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1. Kirk, J. E.: Nutrition and Aging, *Nutrition Rev.* 9:321 (Nov.) 1951.

2. Ohlson, M. A.; Roberts, P. H.; Joseph, S. A., and Nelson, P. M.: Dietary Practices of One Hundred Women from Forty to Seventy-Five Years of Age, *J. Am. Dietet. A.* 24:286 (Apr.) 1948.

3. Kountz, W. B.; Hofstatter, L., and Ackermann, P.: Nitrogen Balance Studies in Elderly People, *Geriatrics* 2:173 (May-June) 1947; Nitrogen Balance Studies Under Prolonged High Nitrogen Intake Levels in Elderly Individuals, *ibid.* 3:171 (May-June) 1948.

4. Kountz, W. B.; Hofstatter, L., and Ackermann, P.: Nitrogen Balance Studies in Four Elderly Men, *J. Gerontol.* 6:20 (Jan.) 1951.

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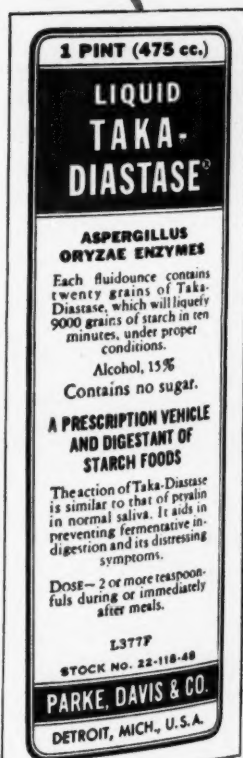
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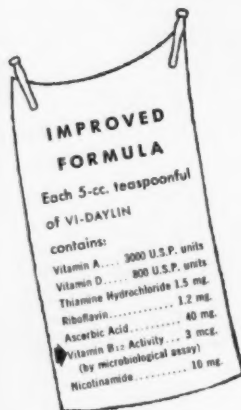


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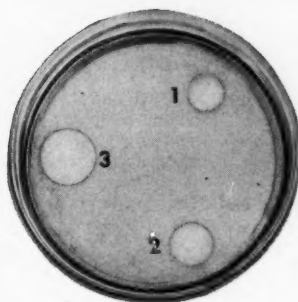
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1. Bralow, S. F., Spellberg, M., Kroll, H., and Nacheles, H.: *Am. Jour. Digest Dis.*, 17:119, Apr., 1950.
2. Hardt, L. L., and Steigmann, Frederick: *Am. Jour. Digest. Dis.*, 17:195, June, 1950.

HEPATIC TESTS IN PRETERMINAL HEPATIC INSUFFICIENCY

JOHN L. SWITZER, M. S., M. D., FREDERICK STEIGMANN, M. S., M. D., JESUS DE LA HUERGA, M. S., M. D., AND FENTON SCHAFFNER, M. S., M. D., Chicago, Ill.

MANN AND OTHERS have stressed the multiplicity of the functions of the liver and its essential position in intermediary metabolism (1, 2). Any natural or induced interference with hepatic function exceeding the hepatic reserve results in hepatic insufficiency, which if prolonged, terminates in coma regardless of the etiology of the hepato-biliary disease.

The determination of the functional efficiency by chemical means is unique in that while all facets of hepatic function may be equally involved in some cases of hepatic disease, in others, one or more of these functions may be disturbed relatively more than the others (2).

In non-terminal patients, attempts have been made to correlate abnormal results of hepatic tests with specific diffuse morphologic changes by means of liver biopsy specimens (3, 4, 5, 6, 7).

Murphy and collaborators (8), Greene (9), and Lichtman (10) failed to show any significant changes in the chemical composition of the blood which could be considered characteristic of hepatic coma or severe insufficiency. The results of the usual laboratory tests were neither characteristic nor of help in elucidating the pathogenesis of the condition nor were they significantly different from precoma findings. Greene found "that in individual cases extreme changes in the chemical composition of the blood may occur but these changes are significant only with regard to the individual case and not to the group as a whole" (9).

It is the purpose of this paper to: 1) list the chemical findings in 32 patients dying from hepatic insufficiency in the light of newer and more refined chemical blood analysis, 2) to enumerate the relationships, if any, of the abnormal results of hepatic tests with specific types of liver injury in the preterminal state, and 3) to determine if there is a significant difference in hepatic tests between those patients who recover from hepatic failure and those who succumb.

MATERIAL AND METHODS

Thirty-two preterminal patients dying from hepatic insufficiency were selected. The mean age was 50.2 years with a range of 20-73 years. There were 20 males and 12 females. Thirty-one were jaundiced at death. In all instances a series of hepatic tests was performed from several hours, 21.8% (7 cases), to a maximum of 15 days, 6.2% (2 cases), with a mean of 3.9 days prior to death.

The tests used and the limits of normality accepted in this study are given in Table I. The selected range

of values was chosen because it represented unequivocally normal values.

The total serum proteins were fractionated into albumin and globulin by the older Howe method (20) and also by a more recent method which more closely mirrors electrophoretic results (21). Gamma globulin was determined turbidimetrically.

The 32 cases of preterminal hepatic insufficiency were further broken down into three categories: 1) acute hepatitis (toxic and viral), 2) cirrhosis, and 3) extrahepatic biliary obstruction.

The duration of hospitalization for all patients averaged 17.9 days with a range of 1-77 days.

TABLE I

HEPATIC TESTS USED AND THEIR NORMAL RANGES

Test	Normal Range
Cephalin flocculation (11)	0 — + +
Thymol turbidity (12)	0 — 4 units
Zinc sulfate turbidity (13)	6 — 12.5 units
Total lipid turbidity (14)	400 — 800 mg. %
Total cholesterol (15)	120 — 220 mg. %
Cholesterol ester ratio (15)	50 + %
Serum esterase (16)	15 + micromoles/ml
Alkaline phosphatase (17)	0 — 4 Bodansky units
Serum bilirubin (18, 19)	0 — 1.0 mg. %
Total protein (20)	6.5 — 8.0 gm. %
True albumin (21)	3.0 + gm. %
True globulin (21)	1.0 — 3.0 gm. %
True A/G (21)	1.0 +
Howe A/G (20)	1.5 +
Gamma globulin (22)	0.7 — 1.25 gm. %
Amino Acids (23)	4.0 — 8.0 mg. %
Blood urea nitrogen (24)	8.0 — 15.0 mg. %
Non-protein nitrogen (23)	20.0 — 40.0 mg. %

RESULTS

The series of hepatic tests in 32 preterminal cases of hepatic insufficiency revealed no specific alterations from those in non-fatal hepatic insufficiency (Table II).

In cases of preterminal hepatitis those tests which markedly reflected hepatocellular dysfunction were most significantly altered. There was, however, a significant elevation of serum bilirubin and a slight elevation of the serum alkaline phosphatase (Table II).

In obstructive jaundice the most markedly altered findings were elevation of alkaline phosphatase and bilirubin. In addition, the most marked reduction of serum esterase was found here (Table II). There was a moderate alteration in the turbidimetric tests together with a reversal of the A/G ratio.

The patients with cirrhosis revealed an elevation in the turbidimetric tests with a fall in the total cholesterol and total lipids. In this group there was a marked protein reversal along with retention of serum

From the Hektoen Institute for Medical Research of the Cook County Hospital, Chicago, Illinois.

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TABLE II.
MEAN VALUES AND RANGES OF VALUES OF TESTS OBTAINED PRETERMINALLY IN HEPATO-BILIARY DISEASES.

Test	Hepatitis (8 cases)			Cirrhosis (16 cases)			Biliary Obstruction 8 cases		
	Mean	Range of Values	Percentage Distribution	Mean	Range of Values	Percentage Distribution	Mean	Range of Values	Percentage Distribution
Cephalin flocculation	3.4	0-2 3-4	12.5 87.5	3.6	0-2 3-4	6.3 93.8	2.3	0-2 3-4	37.5 62.5
Thymol turbidity	10.4	0-5 5-8 8-15 15+	25 25 37.5 12.5	6.6	0-5 5-8 8-15 15+	37.5 25.0 37.5 —	5.1	0-5 5-8 8-15 15+	75.0 — 25.0 —
Zinc sulfate turbidity	21.3	0-6 6-12.5 12.5-20 20+	12.5 25 25 37.5	23.3	0-6 6-12.5 12.5-20.0 20+	6.3 12.5 25.0 56.3	11.4	0-6 6-12.5 12.5-20.0 20+	25.0 37.5 25.0 25.5
Total lipid turbidity	686.0	0-400 400-800 800+	20 40 40	314.0	0-400 400-800 800+	100.0 — —	675.0	0-400 400-800 800+	— 50 50
Total cholesterol	168.0	0-100 100-300 300-450 450+	37.5 50.0 12.5 0	109.0	0-100 100-300 300-450 450+	56.3 43.8 — —	230.0	0-100 100-300 300-450 450+	— 87.5 — 12.5
Cholesterol ester ratio	31.2	0-30 30-50 50+	37.5 62.5 —	36.1	0-30 30-50 50+	37.5 56.3 6.3	26.0	0-30 30-50 50+	87.5 12.5 —
Serum esterase	10.6	0-15 15+	87.5 12.5	9.1	0-15 15+	93.8 6.3	6.9	0-15 15+	100.0 —
Serum alkaline phosphatase	8.1	0-4 4-15 15+	25.0 62.5 12.5	4.9	0-4 4-15 15+	43.8 56.3 —	25.3	0-4 4-15 15+	— 50.0 50.0
Serum bilirubin	30.4	2-8 8+	12.5 87.5	15.2	2-8 8+	43.8 56.3	25.9	2-8 8+	— 100.0
Total protein	6.5	0-6 6-8 8+	25.0 50.0 25.0	6.4	0-6 6-8 8+	25.0 75.0 —	5.81	0-6 6-8 8+	50.0 50.0 —
True albumin	2.4	0-3.5 3.5+	87.5 12.5	1.8	0-3.5 3.5+	93.8 6.3	2.28	0-3.5 3.5+	100.0 —
True A/G ratio	0.67	0-0.6 0.6-1.0 1.0+	50.0 25.0 20.0	0.45	0-0.6 0.6-1.0 1.0+	87.5 6.3 6.3	0.67	0-0.6 0.6-1.0 1.0+	37.5 50.0 12.5
Howe A/G ratio	0.97	0-0.6 0.6-1.25 1.25+	25.0 50.0 25.0	0.82	0-0.6 0.6-1.25 1.25+	43.8 43.8 12.5	1.04	0-0.6 0.6-1.25 1.25+	— 62.5 37.5
Gamma globulin	1.87	0-1.25 1.25-1.50 1.50-2.0 2.0+	37.5 12.5 0 50.0	2.45	0-1.25 1.25-1.50 1.50-2.0 2.0+	6.3 6.3 18.8 68.7	1.47	0-1.25 1.25-1.50 1.50-2.0 2.0+	50.0 12.5 25.0 12.5

bilirubin and a slight elevation of the alkaline phosphatase (Table II).

Blood non-protein nitrogen, blood urea nitrogen and blood amino-acid nitrogen were simultaneously elevated with no reciprocal relationship between the blood amino-acids and the urea nitrogen (Table III)

DISCUSSION:

In accord with previous findings (8, 9, 10) the results of the newer laboratory tests were neither characteristic nor of help in elucidating the pathogenesis of the condition nor were significant differences revealed

between patients with hepatic insufficiency not in coma and those in coma.

In cases of hepatic coma, Murphy and collaborators (8) found that the increased NPN is not of alpha-amino acid nitrogen origin. In five of our cases, alpha-amino acid nitrogen was determined during hepatic coma and revealed values of 3.6 to 4.9 mg.%, all within the normal range. In addition, these authors determined the blood tyrosine (free phenol) fractions which rose but this rise was no greater, as with the other hepatic tests, in hepatic coma than in patients with severe liver disease not in coma. There was a terminal rise in blood NPN correlated with an oliguria which occurred in spite of adequate hydration. The duration of coma in Murphy et al's (8) series of 40 cases ranged from 1-12 days with a mean of 2.8 days.

Bockus reported a marked increase in amino acid nitrogen in severe hepatocellular disease (25). Paralleling the amino-acid increase there was a drop with almost disappearance of the urea nitrogen in markedly severe cases. Blood amino acids are derived from that portion absorbed from the intestine which has escaped deamination and synthesis into protein by the liver plus the amino-acids which result from tissue breakdown which have similarly not undergone deamination and protein resynthesis (26, 27). In hepatic insufficiency the amino-acids are inadequately deaminized causing a change in the normal BUN/amino-acid N ratio of 2:1 (26). High values of amino-acid nitrogen are not ordinarily found in chronic hepatic disease such as cirrhosis and chronic obstructive jaundice because of the large functional reserve and marked regenerative power of the liver (26). In this series, it was found that to the contrary there were parallel NPN, BUN, and amino-acid elevations and with the increase in amino-acids there was no corresponding drop in urea nitrogen. As previously reported, there was no significant difference

in results between the three types of liver disease enumerated (28).

In accord with the data of Norcross, et al, in non-terminal patients it was found that the serum bilirubin and alkaline phosphatase were elevated in cirrhosis and biliary obstruction (7). Popper, Waldstein, and Szanto found that of the hepatic tests studied, increased cephalin flocculation and thymol turbidity appeared best to indicate the presence of diffuse hepatic cell damage in cirrhosis; this was similarly seen on these cases with no preferential alteration due to the preterminal state (29).

Seven patients in our series were treated with aureomycin with a maximum total dose of 20 grams orally in 11 days and 3 grams intravenously in 3 days in separate instances (30). In view of the report of Lepper, et al., that aureomycin therapy caused a slight decrease in liver function by serial tests with particular reference to the turbidimetric tests (31), the data of these seven cases were analyzed to determine if any alterations in liver function could be attributed specifically to this drug. No changes were noted and if any slight variations were present, they were overshadowed by the much greater changes due to the primary disease.

It has been suggested that many of the symptoms of patients with liver damage may be due to an accumulation of acetylcholine in the blood following a fall in the serum esterase. However, Wilson and Walshe (32) infused human patients with hepatic insufficiency with human serum rich in cholinesterase and raised the serum esterase to within normal levels without affecting the depth of consciousness of patients in coma. In our series, serum esterase activity was decreased in all three categories of hepatic disease with the greatest reduction being noted in those patients with obstructive jaundice. While the degree of coma of these patients was not graded clinically, it is felt that all of the collected data throw no further light upon the pathogenesis of hepatic coma.

TABLE III.

MEAN VALUES AND RANGES OF BLOOD NON-PROTEIN, UREA AND AMINO-ACID NITROGEN IN PRE-TERMINAL CASES WITH VARIOUS HEPATO-BILIARY DISEASES

Category	Number of Determinations	Test	Mean mg. %	Range mg. %
1. Total preterminal unclassified	27	N.P.N.	90.0	27.0-220.0
	27	B.U.N.	57.3	5.6-128.8
	27	amino-acids	13.1	8.2- 28.6
2. Hepatitis	6	N.P.N.	92.9	27.0-182.4
	6	B.U.N.	55.7	5.6-128.8
	6	amino-acids	16.3	8.2- 28.6
3. Obstructive jaundice	6	N.P.N.	94.3	53.6-152.0
	6	B.U.N.	68.6	26.0-125.2
	6	amino-acids	16.3	8.4- 15.9
	15			
4. Cirrhosis	15	N.P.N.	87.4	30.0-220.0
	15	B.U.N.	53.4	12.8-126.8
	15	amino-acids	12.3	8.61-19.3

SUMMARY:

In spite of the refinement of hepatic tests, no new light could be shed upon the pathogenesis of hepatic coma. In addition, it is stressed again that the results of hepatic tests in preterminal hepatic insufficiency with coma are not significantly different from those obtained in cases of hepatic insufficiency which recover. Blood non-protein nitrogen, urea nitrogen, and the blood amino-acids were simultaneously and significantly elevated.

The suggestions of Dr. Hans Popper in the performance of this study are greatly appreciated. Thanks are due to Miss Lois Davis for her help in the statistical analysis of the data.

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DIFFERENTIAL DIAGNOSIS OF HEPATITIS AND LIVER CIRRHOSIS BY MEANS OF CHOLECYSTOGRAPHY*

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AS OUR knowledge of the central position of the liver in many metabolic and other processes has advanced, the possibilities of a detailed analysis of various liver diseases have also progressively increased. The accurate description of the condition in disease of this organ with its numerous functions is possible to a remarkable extent, but it requires the help of extensive laboratory facilities. An independent practitioner, who, nevertheless, is often charged with the most difficult diagnostic task in determining the cases of liver disease, has still to make the diagnosis without the help of a highly organized laboratory. With the help of a good anamnesis and simple routine examination, it is

generally possible to differentiate diffuse lesions of the liver from for instance other diseases associated with a pathological increase in the urinary excretion of urobilinogen and urobilin (sometimes bilirubin) typical of liver diseases, such as gallbladder affections, local processes affecting the bile ducts or liver, and diseases associated with haemolysis. However, it is often more difficult to judge to which type of diffuse liver lesions an actual case belongs. Although this differentiation is in general easy with the help of simple clinical routine methods when the cases are typical, it may still be difficult for a physician working without the help of a laboratory, if some characteristic symptoms are unclear. An attempt is made in the following treatment to study whether this diagnostic problem can be solved to any extent with the help of an X-ray examination of the gallbladder.

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CHOLECYSTOGRAPHY AS A LIVER FUNCTION TEST

It was already clear to the inventors of cholecystography, Graham and his co-workers (1, 2), when they published their discovery in 1924, that the secretion of the radio-opaque dye they used, the sodium salt of tetrabromphenolphthalein, into the bile ducts and gallbladder was dependent on the function of the liver. In 1913 Rowntree et al. (3) had already demonstrated that the secretion of phenoltetrachlorophthalein from blood into the bile ducts was correlated with the functional capacity of the liver. The relations of liver function and cholecystography have later been the subject of several studies, and the general conclusion has been that cholecystography is usually unsuccessful in connection with liver cirrhosis. However, these investigations date from early periods, and in those times it was not possible to correlate the results of cholecystography with other liver function tests. The relation of cholecystography to other well-esteemed liver function tests has been studied only in the case of the bromsulphthalein test. Among these studies, that of Blomström and Sandström (4) is well known. These authors demonstrated that if the retention of bromsulphthalein is at or above 40 per cent, the shadow of the gallbladder is not observable in the cholecystography; if the retention is from 30 to 40 per cent, the appearance of a radiologically observable shadow is uncertain; if the retention remains below 30 per cent, a distinct shadow of the gallbladder will be observed. Present opinion is expressed e. g. Bockus (5), who states that if the patient has retained as much as 25 per cent of the bromsulphthalein dye in the blood one-half hour after its injection, it is possible to demonstrate a satisfactory shadow of the gallbladder. Thus, it has been demonstrated experimentally that the results of cholecystography are definitely correlated with those of the bromsulphthalein test. Theoretically, these tests are closely related, for the dyes used in cholecystography are both physically and chemically related to sodium tetrabromphenolphthalein which is used in the bromsulphthalein test, and the essence of both tests is the ability of the liver to eliminate the dye from the blood into the bile. On the other hand, the bromsulphthalein test is being regarded as one of the best, if not the best among the liver function tests. Thus Lichtman (6) states in his monograph in 1949: "Bromsulphthalein test is of utmost value in the diagnosis of disturbance of the excretory function of the liver." This test has, of course, no value in connection with severe jaundice (obstruction of the bile ducts or a severe hepatocellular process impeding bile flow), when the bile cannot flow freely through the liver, for reasons independent of the functional capacity of the hepatic cells. Exactly similar observations have been made on cholecystography. In cases of hepatitis for instance the highest value of the icterus index compatible with the radiological demonstrability of the gallbladder in cholecystography is being assessed at 1/40-1/80 (4, 7, 8).

In addition to severe jaundice, as mentioned above, other possible sources of error have been advanced as limiting the value of cholecystography as a liver function test: (1) When the dye is given per os, as it is now generally administered, its intestinal absorption may be disturbed. (2) The flow of bile (and also

of the dye) into the gallbladder may be prevented, e. g. by an obstruction of the cystic duct or when the gallbladder is lacking (operation, aplasia). (3) The normal concentrating capacity of the gallbladder is decreased. (4) Cholecystography does not always succeed in pernicious anemia, exophthalmic goitre, and sometimes not in diabetes mellitus.

When those easily excluded cases are omitted in which stenosing processes, like pyloric stenosis, occur in the digestive tract, or when the patient vomits the dye for some other reason, or if he or she has severe diarrhea, a disturbance in the intestinal absorption of the dye remains a rarity when the modern radio-opaque dyes are being used, as has been demonstrated in several studies in which the administration of the dye through the intravenous route has been compared. The possibilities mentioned under (2) and (3) must, of course, be noticed in practice. However, these disturbances are not very common, not even in connection with the affections of the gallbladder. For instance, among 33 cases of cholelithiasis and cholecystitis treated in our clinic, there were only five in which the gall bladder could not be filled at all in connection with cholecystography (in three of these, a positive stone shadow was observable). In 11 cases of this group, the gallbladder had filled less than normally. As to point (4), it has been considered that the relatively frequent failure of the cholecystography in pernicious anemia depends on a disturbance in the hepatic function in this disease (9). Since there occur quite regularly changes also in other liver function tests in connection with exophthalmic goitre (10, 11) and sometimes, if less often, also in diabetes mellitus, these failures cannot be regarded as negative findings when assessing the value of cholecystography as a liver function test—rather the contrary.

MATERIAL

The material consists of cases of acute and subacute hepatitis and of portal liver cirrhosis treated in our clinic during the years 1948-1951 and subjected to cholecystography.

The number of patients suffering from hepatitis was 23, of which 11 were male and 12 female. The mean age in the group was 43.8 years. The examination at the hospital and the course of the disease have settled the diagnosis.

The number of cases of liver cirrhosis was similarly 23, of which 16 were male and 7 female. The mean age was 55.9 years. The diagnosis was confirmed, in addition to the clinical examination, by a biopsy taken during laparotomy in 6 cases, and later at autopsy in 7 additional cases.

As a control, cholecystography was made in 44 patients suffering from peptic ulcer: 26 of these were male and 18 female. The mean age in this group was 46.3 years.

METHOD

Cholecystography was made on all of the patients in the normal manner, by administering the dye per os. In the majority of the cases, β -4-hydroxy-3, 5-diiodophenyl- α -phenyl propionic acid was used, and in some, the employed dye was the sodium salt of tetra-

iodophenolphthalein. The radiography was carried out 16-18 hrs. after the ingestion of the dye, the patient fasting all the interval. As the intensity of the shadow of the gallbladder depends on many factors, technical among them, no attempt was made to analyse it exactly, and it was decided to use the practically easiest though somewhat inaccurate description: "normal filling," "poor filling," "no filling." If the shadow of the gallbladder was visible, its behaviour on the ingestion of a fat meal was observed in the usual manner.

RESULTS

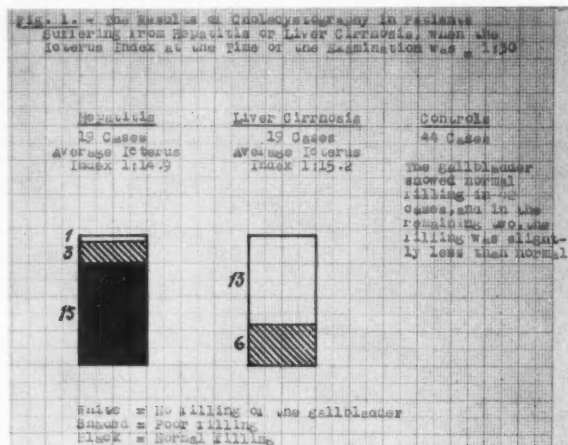
Figure 1 shows the filling of the gallbladder in connection with cholecystography in the groups of hepatitis and of liver cirrhosis. However, these cases have been omitted in which the icterus index exceeded 1/30, since, as already mentioned, the filling of the gallbladder during severe jaundice may be prevented for reasons independent of the function of the hepatic cells. Thus, four patients were discarded from the group of hepatitis and similarly four patients from the group of liver cirrhosis. In the discarded cases of hepatitis, the icterus index was 1/40, 1/59, 1/140, and 1/180. In the two last mentioned, there was no radiologically observable filling in the gallbladder; in the remaining two, the filling was less than normal. In one of these cases the emptying was normal, in the other it was delayed. In the omitted 4 cases of liver cirrhosis, the icterus index was 1/40, 1/48, 1/70, and 1/90, and in none of these could the filling of the gallbladder be observed radiologically.

tion of the dye. In the remaining three cases of liver cirrhosis, only a slight change in the shadow of the gallbladder could be observed in connection with the fat meal. In the hepatitis group, the emptying of the gallbladder was normal after a fat meal in 17 of those 18 patients in whom the shadow of the gallbladder was observable.

The distinction between the groups of hepatitis and liver cirrhosis becomes still more marked, if the case of hepatitis showing no filling of the gallbladder is subjected to a more detailed analysis. Although the disease had the typical character of hepatitis, so far as its course and the laboratory examination showed (possibly inoculation hepatitis), it is most probable that the patient was suffering at the same time from cholelithiasis as well, for he had at times during five years experienced attacks typical of cholelithiasis, and had been under hospital treatment for them three times; operative treatment was not attempted however because of the high age (71 years), the poor condition and the relatively rapid disappearance of the symptoms in connection with the attacks.

Table 1 and Table 2 show the relation of the results of cholecystography to some other liver function tests made on the same patients.

As the tables 1 and 2 show, the results of the cholecystography seem to correspond best with the results of the Takata-Ara test. No similar correspondence could be observed with the mercuric chloride test, with the



As may be observed in Figure 1, the filling of the gallbladder is considerably poorer in liver cirrhosis than in hepatitis, while the icterus index is practically the same. This finding corresponds well with the results of the bromsulphthalein test. Moreover, it is to be noted that among those six cases of liver cirrhosis which were described as showing "poor filling," three exhibited a positive shadow in the region of the gallbladder in the control picture before the administration of the dye. It was very uncertain whether the intensity of this shadow increased owing to the ingestion

of the dye. In the remaining three cases of liver cirrhosis, only a slight change in the shadow of the gallbladder could be observed in connection with the fat meal. In the hepatitis group, the emptying of the gallbladder was normal after a fat meal in 17 of those 18 patients in whom the shadow of the gallbladder was observable.

TABLE 1
RELATION OF CHOLECYSTOGRAPHY TO SOME LIVER
FUNCTION TESTS

19 Cases of Hepatitis (Icterus Index < 1/30)	"No Filling" of the Gallbladder		"Poor Filling"		"Normal Filling"	
Number of Cases	1		2		15	
Average Icterus Index	1:13		1:14.7		1:12.7	
	Normal	+	Normal	+	Normal	+
Takata-Ara	1	0	3	0	12	3
Mercuric Chloride	1	0	2	1	6	5
Thymol Turbidity	0	1	0	3	2	10
Zinc Sulphate Turbidity	0	0	0	0	2	2
Alkaline Phosphatase	1	0	2	1	5	0
Albumin/Globulin Ratio	0	0	2	0	2	2
19 Cases of Liver Cirrhosis (Icterus Index < 1/30)						
Number of Cases	13		6		0	
Average Icterus Index	1:15.9		1:12.2			
	Normal	+	Normal	+		
Takata-Ara	0	13	1	5		
Mercuric Chloride	0	11	0	6		
Thymol Turbidity	1	10	1	5		
Zinc Sulphate Turbidity	0	3	0	5		
Alkaline Phosphatase	3	7	2	4		
Albumin/Globulin Ratio	1	7	0	4		
The positivity of the tests ¹² :						
Mercuric Chloride Titration	1.40ml					
Thymol Turbidity	0.15 ext.					
Zinc Sulphate Turbidity	0.20 ext.					
Alkaline Phosphatase	12 U					
Albumin/Globulin Ratio	1.5					

TABLE 2
RELATION OF CHOLECYSTOGRAPHY TO SOME LIVER
FUNCTION TESTS

Intensity of the Gall- bladder Shadow	Takata-Ara		Mercuric chloride		Thymol turbidity		Zinc Sulph. turbidity		Phosphatase		Alb./Glob. ratio	
	+	-	+	-	+	-	+	-	+	-	+	-
"Normal Filling"	12	3	6	5	12	10	1	2	5	0	2	2
"Poor Filling"	4	5	2	7	1	8	0	5	4	5	2	4
"No Filling"	1	13	1	11	1	11	0	3	4	7	1	7

CONCLUSIONS

From the above, it appears evident that in connection with slight jaundice (icterus index below 1/30), the shadow of the gallbladder appears essentially more dis-

tinctly in cases of hepatitis than in those of liver cirrhosis, even to such a degree that if the filling of the gallbladder with the dye is normal, liver cirrhosis can be excluded. In the sources of error mentioned above, in particular when affections of the gallbladder have been taken into account, a lacking gallbladder shadow may be considered as suggesting liver cirrhosis.

When cholecystography is employed in assessing the function of the liver, it has, of course, to be noted that it gives information on one aspect only, mainly of the hepatic secretory and excretory function. Although it may be argued that this examination gives a rather one-sided picture of the functional abilities of this organ the same claim has been made about the bromsulphthalein test, it is, nevertheless, evident that this function is quite central among the many hepatic functions and in addition, specific to the liver. For example the tests based on changes in the proteins, which have lately gained increasing favour, may be affected, as is well known, by factors influencing the protein metabolism independently of the liver, and thus their specificity suffers.

According to our opinion, cholecystography may in many cases give such a selective picture regarding the hepatic function that it helps in the differential diagnosis of various diffuse hepatic affections, as of hepatitis and liver cirrhosis. As a practical method, cholecystography ought to be given more value in this respect than has occurred up to now, in particular, if the help of special laboratories can not be obtained in the examination of the patients. This examination is considered to have no untoward effects on the patient.

SUMMARY

19 patients suffering from acute or subacute hepatitis and 19 cases of liver cirrhosis were subjected to cholecystography with dye given per os in the usual manner, at a time when the icterus index was below 1/30. The shadow of the gallbladder appeared normal in 15 cases of hepatitis, was less pronounced than normal in 3 cases, and in one case in which the patient suffered also from cholelithiasis, it did not appear at all. In the cases of liver cirrhosis, the shadow of the gallbladder did not appear normal in any of the cases; in 6 of the cases a slight shadow was observable, and in 13 cases, no shadow could be observed. A comparison with some hepatic function tests also suggested that cholecystography may be of some help in the differential diagnosis of hepatitis and liver cirrhosis.

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EFFECT OF SODIUM CARBOXYMETHYLCELLULOSE ON THE BLOOD CELLS*

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IN VIEW OF the recent therapeutic usage of sodium carboxymethylcellulose (sodium cellulose glycolate) in such diverse clinical conditions as constipation (1, 2, 3), peptic ulcer (4, 5), in the modification of digoxin action (6), and in controlling nausea and vomiting caused by terramycin (7), a thorough study of the effects of sodium carboxymethylcellulose on the blood cells was thought to be of value. Since this substance has been used as a thickener for foodstuffs since

1924 (5) and is finding increased use in the food industry as a stabilizer, a study in patients that could be given large doses of the drug and could be carefully followed with a serial blood studies seemed particularly desirable.

METHOD OF STUDY

The subjects were selected from among the patients of an institution for chronic diseases. The patients chosen did not have anemia or constitutional disease affecting the hematopoietic system with one exception, a patient with polycythemia of moderate degree. Some of the patients were ambulatory, others were bedridden. There were in constant attendance either registered or practical nurses who assisted in the distribution of the medication, in addition to their regular duties. In this way a careful check of drug administration and ingestion was possible. In the control or foreperiod of two weeks two complete blood counts per

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TABLE I

Case No.	Sex	Age	Disease	Control Period			End of Study			Total Dose (GMS)	Remarks
				R.B.C. X10 ⁶	Hct. VOL %	W.B.C. X10 ³	R.B.C. X10 ⁶	Hct. VOL %	W.B.C. X10 ³		
1.	M	71	Paget's Disease & Osteoarthritis	5.2	42.0	11.2	5.3	44.5	10.85	1940	Constipation relieved
2.	M	42	Birth Injury	5.3	44.0	8.7	5.5	45.5	6.25	1940	
3.	M	60	Cerebral Atrophy	5.5	47.5	8.6	5.3	43.5	10.2	1940	
4.	M	49	Parkinson's Disease	5.2	43.0	6.9	5.4	47.5	6.8	1940	
5.	F	56	Multiple Sclerosis	4.7	40.0	4.6	4.5	40.0	8.2	1940	
6.	F	80	Fractured Femur	5.2	42.0	7.5	5.4	43.5	7.1	1940	
7.	F	79	Osteoarthritis	5.1	47.0	6.6	5.8	45.0	7.6	1940	
8.	M	82	Arteriosclerosis	5.2	44.1	9.0	4.8	40.0	7.8	1940	
9.	F	75	Arteriosclerosis	4.7	35.0	7.3	4.3	38.0	5.2	1940	
10.	F	68	Parkinson's Disease	4.7	39.1	6.1	5.1	42.0	8.2	1940	Constipation relieved
11.	F	68	Metastatic Carcinoma of uterus	4.4	40.0	5.0	4.7	40.5	9.6	1940	
12.	M	67	Diabetes Mellitus	5.9	47.0	6.9	6.0	47.5	6.0	1806	Transient diarrhea
13.	F	61	Poliomyelitis	5.1	40.6	5.0	5.2	41.0	7.6	1346	Diarrhea—dose reduced
14.	F	70	Osteoarthritis	4.8	40.0	7.2	5.3	44.5	7.5	1268	Diarrhea—dose reduced
15.	M	63	Birth Injury	5.1	44.0	8.7	5.4	42.5	7.6	1262	Dose reduced
16.	M	27	Friedreich's Ataxia	5.7	44.0	5.8	5.4	45.0	11.2	1110	Intermittent diarrhea
17.	F	58	Multiple Sclerosis	5.3	42.0	5.8	5.4	42.0	8.5	982	Diarrhea—dose reduced
18.	F	80	Transverse Myelitis	5.1	39.5	6.7	5.2	41.5	9.6	866	Abdominal discomfort—dose reduced
19.	M	79	Polycythemia Vera and Buerger's Disease	7.5	59.5	10.9	7.1	62	12.1	786	Transferred to another hospital
20.	F	56	Osteoarthritis	5.2	43.0	9.9	5.2	22.0	7.4	694	Refused to continue
21.	F	80	Osteoarthritis	4.6	41.0	5.8	5.1	41.5	8.0	460	Refused to continue
22.	M	78	Parkinson Disease	5.1	41.5	7.7	5.3	42.5	7.8	440	Refused to continue

week were done. A similar number of urinalyses were performed. After the beginning of drug administration, a complete blood count was done every two weeks until the cessation of the test period. In selected patients, bone marrow study was done early in the period of drug administration and at the completion of the study.

A complete blood count consisted of red blood cell count (two counts were done and averaged for the result), white blood cell count and differential smear, hematocrit, hemoglobin and buffy coat determinations. Red and white blood cell pipettes certified by the United States Bureau of standards, a Fisher Electro-Photometer Hemoglobinometer, and Wintrobe hematocrit tubes were used. All of the laboratory work performed was supervised by Dr. Charles E. Rath, Director, Hematology Laboratory, Georgetown University Hospital. Each of the patients had been examined prior to the institution of drug administration and diagnosis recorded.

A daily dose of 10 grams of sodium carboxymethyl-

cellulose given in the form of wafers each containing 2 grams of the drug was started in each patient. Eleven patients continued this dose without change for the test period of six months. In other cases reductions in dose had to be made, usually because of diarrhea, loose bowel movements, or lack of cooperation on the part of the patient in continuing prolonged therapy with a daily large dose.

PREVIOUS STUDIES ON THE BLOOD IN ANIMALS AND HUMANS

Rowe, Spencer, Adams and Irish (8) studied the effect of feeding sodium carboxymethylcellulose in varying dosages on rats for a period of eight months. No discernible ill effects from large amounts could be found as determined by growth curves, organ weights, gross observations and histopathological examinations. While the blood cells were not specifically studied, the spleen was not affected. Shelanski and Clark (9) examined the blood of 10 rats and 10 guinea pigs during and

TABLE 2

Case No. 2

Age 42

Diagnosis: Injury at birth, muscle incoordination, eyes and hands.

		Blood											
		Diff-Smear %										PMN	
Date	Medication	HGB Gms.	RBC Millions	WBC	Hematocrit	Buffy Coat	Lymphs	Mono.	Eos.	Baso.	Mature	Bands	
5-2-51	Control	16.6	5.35	9,200	46	.6	22	1	2		75		
5-15-51	Control	16.4	5.34	8,100	42	.5	22	1			77		
5-25-51	Control	15.8	5.25	8,750	44	.6	25		3		72		
5-5-51	Control	14.8	5.46	7,400	47	.5	26	1	2		71		
7-20-51	10 g/day	17	5.61	7,700	46.5	.5	24	3			73		
8-1-51	10 g/day	16.2	5.60	8,500	45	.5	21	3	2	1	71	2	
8-21-51	10 g/day	16.5	5.79	8,050	48	.6							
9-11-51	10 g/day	16.5	5.85	7,750	47	.6	18				82		
9-25-51	10 g/day	16.4	5.65	7,500	45	.6	20	2	3	2	72	1	
10-8-51	10 g/day	15.2	5.40	7,800	46.5	.5	22	1	1		76		
10-22-51	10 g/day	15.8	5.39	7,250	45.5	.5	21	2	1	1	75		
11-5-51	10 g/day	15.5	5.40	8,250	46.5	.5	26		3	1	70		
11-22-51	10 g/day	16	5.46	7,500	45	.5	28	2	1	1	68		
12-6-51	10 g/day	15.4	5.39	5,500	43	.5	16	3			81		
12-20-51	10 g/day	15.2	5.60	8,000	43.5	.5	24	4	2		70		
1-3-52	10 g/day	15.6	5.55	6,250	45.5	.5	20	3	1		77		
		Urine											
		Per HPF Centrifuged											
Date	Color.	Sp. Gr.	React.	Alb.	Sugar	Rbc.	Wbc.	Casts	Crystals				
5-17-51		1.025	5	+	—	1-2	occ.	occ.	hyaline				
5-24-51		1.020	5	0	—	1-2	1-2	occ.	hyaline				
5-29-51		1.022	5	0	—	1-2	1-2	occ.	hyaline				
1-11-52		1.020	5	0	0		0-2	occ.	1 hyaline cast.				

ADDITIONAL REMARKS—Dosage, etc. Patient started July 5th 10 g/day through January 15th—no complications.

BONE MARROW 6-25-51 Sternum—Cellular preparation which shows an essentially normal distribution of cells. Megakaryocytes numerous. Plasma cells slightly increased. No abnormal cells found. Impression: Essentially normal marrow. 1-16-52 Sternum—Cellular preparation which shows no change from previous marrow. Grade II marrow iron. Impression: Normal bone marrow.

Total Dose
1940 Grams

after a six month feeding study and no evidence of pathology was found. Urinalyses also showed no changes. In white rats fed one gram of sodium carboxymethylcellulose daily per kilogram of body weight for over two years, no deviations from the control monthly blood studies of hemoglobin determinations, red and white blood cell counts were noted. The study also indicated that sodium carboxymethylcellulose was not absorbed from the intestinal tract and was eliminated almost completely.

Blake (2) reported the use of two to four grams of sodium carboxymethylcellulose daily in 17 human subjects who had determinations of hemoglobin, red blood cell count, white blood cell count and differential smear before and after treatment which extended from four to nine months. No deviations that could be considered physiologically significant were noted. This report is apparently the only one available in which a specific study of the effect of the drug on the blood cell constituents of human patients was undertaken.

RESULTS

Table I lists in brief form the results of the study. The complete protocol of a typical case is shown in Table II. The values of the red blood cell count, white blood cell count and hematocrit showed no significant variations from the control period after administration of sodium carboxymethylcellulose for six months. The total dose ranged from 440 to 1940 grams. Differential smears of the white blood cells also revealed no abnormal changes. No patients on the drug experienced either an anemia or a leukopenia. Bone marrow studies of three patients during the early part of the test period as compared to similar studies at the end of six months of drug administration revealed no changes. An additional three patients had bone marrow studies at the end of the six month test period and the results of these studies were within normal limits.

It is to be noted in Table I that despite the assorted types of diseases that these chronic patients had, the control blood studies were essentially all normal. We attribute this to the excellent dietary management and abundance of food offered these chronically ill patients in the institution in which the study was done. One patient with polycythemia vera received the drug without any change in his blood picture. The urinalyses at the completion of the study revealed no significant changes in comparison with those done during the control period.

In seven of the patients it was necessary to reduce the dose of sodium carboxymethylcellulose usually because of diarrhea, abdominal discomfort, or a feeling of urgency to have a bowel movement. The diarrhea consisted of an increase in the number of bowel movements, varying from two to six movements daily. The stools were noted to be loose without any blood, pus, or mucous being observed. It was also found that ambulatory patients did not seem to be troubled by this

difficulty whereas the bedridden ones were. Most of these patients were able to tolerate doses of six to eight grams daily without further difficulty. This is not surprising in view of the 10 gram daily dose used when it is recognized that the usual dose used for laxative effect, due to its hydrophilic properties varies from two to four grams daily.

Since many of these patients had been chronically constipated, it was interesting to observe, incidentally, the satisfactory relief obtained by some patients. Tolerance for the larger doses was much better in the previously constipated patients. No changes in any of the diseases that the patients had, as listed in Table I, could be discerned clinically.

SUMMARY

1. A large daily dose of sodium carboxymethylcellulose was given to a group of patients for a six month period.
2. Careful study of the effect on the blood cell constituents was made.
3. No significant effect on the blood cell constituents could be ascertained as resulting from the administration of sodium carboxymethylcellulose. Bone marrow was also unaltered in a small group of patients in which such study was done.
4. Many of the patients tolerated much larger doses than are ordinarily used therapeutically without ill effect.

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THE SURGICAL TREATMENT OF PORTAL HYPERTENSION

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THE PROBLEMS posed by portal hypertension have interested clinical and experimental investigators for many years. Von Eck (1) performed the first portacaval anastomosis in dogs in 1877. A side to side technique was utilized, and this shunt has become known as the Eck fistula. Whipple (2) has observed dogs with Eck fistulas for periods as long as 8 years. These animals had occasional disturbances which were attributed to disturbed protein metabolism, but they maintained a satisfactory state of health. Prior to 1945, occasional attempts had been made to perform portal-systemic shunts in cases of portal hypertension, but small tributaries of the portal vein and inferior vena cava were usually employed, and thrombosis frequently developed at the site of anastomosis. In 1945, reports of successful shunts appeared (3, 4), and a renewed interest was stimulated in this field.

THE PORTAL VENOUS SYSTEM

The portal vein receives 2 large tributaries, the superior mesenteric and splenic veins, in addition to several smaller vessels. A common pattern is depicted in Figure 1, but variations are frequently observed. Since the configuration is often irregular, it is important in every case of portal hypertension to ascertain at operation exactly which pattern prevails, and just where the obstruction is. The portal vein breaks up into smaller tributaries within the liver, and together with branches of the hepatic artery and bile duct, these vessels course between the hepatic lobules. The portal blood passes through the capillaries of the hepatic lobules, through the central vein of the lobule, and then to the inferior vena cava via the hepatic veins. The portal and hepatic veins and the inferior vena cava are devoid of valves. The flow of blood from the portal to the hepatic veins is aided considerably by the negative pressure within the vena cava.

The normal venous pressure within the portal system varies from 60 to 140 mm. of water, according to Whipple (5), and from 140 to 220 mm. of saline, according to Bellis (6). There has been no standardized method clinically for recording this pressure, which accounts for the variations noted in different reports. If the pressure is more than 200 mm. of water, the patient is assumed to have portal hypertension. When the obstruction to the portal flow is suprahepatic, an increase in portal pressure does occur, but it usually does not cause the development of esophageal varices and gastrointestinal bleeding. When clinically significant esophageal varices are present, they are invariably a consequence of hepatic or intrahepatic portal vein obstruction.

INTRAHEPATIC PORTAL OBSTRUCTION

Any form of extensive liver pathology may conceivably cause an elevation of portal pressure, but this intrahepatic type of obstruction is usually associated

with cirrhosis of the liver. It is generally assumed that the intrahepatic fibrosis compromises the caliber of the portal vein branches, but this has not been established conclusively. It is true that these vessels are more vulnerable to pressure than the branches of the hepatic artery or bile duct because of the thinness of their walls and the lower pressure within their lumina. However, in many cases there is an extreme degree of liver scarring with minimal portal hypertension, and in other patients there is relatively little fibrosis but marked elevation of the portal pressure. Herrick's (7) studies have revealed numerous communications between the portal vein branches and the hepatic arteries within the liver, and have demonstrated pronounced effects on portal pressure by means of slight increases in hepatic artery pressure in the cirrhotic liver. In the normal liver, there was a rise of portal pressure of 1 mm. of mercury for every 40 mm. elevation of arterial pressure. In cirrhosis, a 1 mm. rise of portal pressure occurred for every 6 mm. elevation of arterial pressure. McIndoe (8) has been unable to confirm these observations, but did note that only 13 per cent of the fluid perfused through the portal vein in cirrhosis could be recovered from the hepatic vein. The remainder was dissipated through collateral channels. He concluded that the portal hypertension developed from a gradual shutting off of portal blood from the hepatic cells as interlobular fibrosis developed. It has been proposed recently (9) that the regenerating liver nodules which develop in cirrhosis may play the important part in occluding the portal vein branches. This may explain the previous discrepancies noted between the extent of liver fibrosis and the height of portal pressure.

EXTRAHEPATIC PORTAL OBSTRUCTION

In this group of cases, the obstruction is usually in the portal or splenic vein. Although it is frequently referred to, thrombosis of the distal portion of the splenic vein is relatively rare. If it were present, it would cause an enlarged spleen, anemia, leucopenia, and the picture of hypersplenism. Splenectomy alone would be the indicated procedure. However, if the thrombosis or obstruction extends proximal to the entrance of the coronary vein into the splenic, then a splenectomy would not remove the obstruction and the high portal pressure would persist.

When a block in the portal vein exists, it is usually due to thrombosis, external compression, or cavernomatous transformation of this vessel. It is apparent that there may be a variety of underlying factors in each of these three categories. Whereas the "intrahepatic group" consists predominantly of individuals with cirrhosis, the patients with extrahepatic obstruction are frequently in the younger age groups and their liver function is usually normal.

EXPERIMENTAL ATTEMPTS TO PRODUCE PORTAL HYPERTENSION

The study of portal hypertension would be greatly

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facilitated if a satisfactory method of producing this condition in animals could be evolved. A great deal of experimental work along these lines has been performed, but it has been extremely difficult to produce a picture of portal hypertension in dogs which is identical to that seen clinically. There are 3 general methods of approach. The first is by producing a chronic cirrhosis of the liver. This can be accomplished by repeated injections of finely powdered silica into the portal vein (10). The animals develop liver cirrhosis, splenomegaly and venous congestion, but the technique is difficult and the resulting clinical picture not identical to the clinical syndrome. Other investigators have attempted to produce an extrahepatic portal block by cicatricial constriction of the portal vein by means of cellophane fibrosis (11). However, in a large number of cases in which the portal vein is divided after preliminary constriction, the pressure does not rise to the expected level, no permanent splenomegaly results, and esophageal varices do not develop. The retroperitoneal vessels are so adequate in dogs that there is apparently an insufficient stimulus for the development of esophageal varices. The third experimental method by which portal hypertension is produced is by suprahepatic occlusion of the inferior vena cava. Ascites usually develops, probably as a result of passive congestion of the liver, but this procedure does not reproduce the clinical picture of portal hypertension. Monkeys usually survive even immediate ligation of the portal vein because of their extensive collateral circulation (12), and are thus not suitable for this experimental work.

OPERATIVE TREATMENT

Since it is so difficult to produce in animals the typical picture of portal hypertension, one is unable to assess experimentally the relative merits of the various operations which have been proposed for this condition. Numerous procedures have been advocated, but few have withstood the test of time. Probably the crux of the problem is whether the operation performed reduces the high pressure in the portal system. It is true that hypertension is merely secondary to liver disease or other pathology, but many patients succumb directly as a result of the elevated pressure. It has been reported (13) that 40 per cent of the patients who have hemorrhage from esophageal varices die within one month of the first hemorrhage. If the portal pressure can be reduced, a palliative effect is achieved, and this allows time for further regeneration of the liver.

The operations which have been proposed for the treatment of portal hypertension may be classified as follows (14):

1. Drainage procedures: (a) Insertion of button into abdominal wall; (b) saphenoperitoneal anastomosis; (c) pyloperitoneal anastomosis.
2. Direct treatment: (a) Injection of esophageal varices; (b) ligation of varices; (c) esophagogastric resection; (d) mediastinal packing.
3. Portal-systemic venous shunts: (a) Omentopexy; (b) portacaval, splenorenal and other venous anastomoses.

Crosby and Cooney (15) described several patients with marked ascites who were treated by the insertion of

a glass button into the lower abdominal wall. This allowed the escape of ascitic fluid into the subcutaneous tissue. The patients were considered improved, but the longest period of postoperative observation was 11 months. Lord (16) added 2 modifications: The creation of a large subcutaneous pocket and the removal of fascia overlying the abdominal muscles. The reports describing this mode of treatment are thus far inconclusive. The method is only palliative and does not attack the basic problem since it does not affect the portal pressure. The ascitic fluid is merely diverted to other channels. Occasional reports of sapheno-peritoneal and pyelo-peritoneal anastomoses have appeared, but these methods have never been widely accepted. It is questionable whether the anastomotic openings created remain patent.

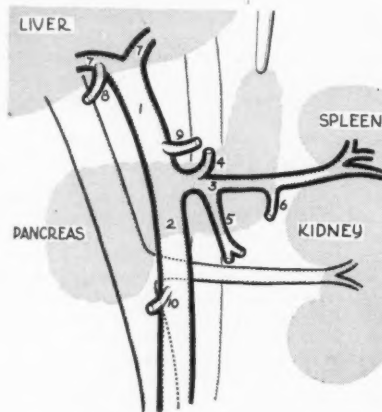


Figure 1: Schematic drawing of the extrahepatic portal system: 1. Portal vein; 2. superior mesenteric vein; 3. splenic vein; 4. coronary vein; 5. inferior mesenteric vein; 6. left gastro-epiploic vein; 7. intrahepatic portal vein branches; 8. cystic vein; 9. pyloric vein; 10. right gastro-epiploic vein. This is a common pattern, but there are many variations.

The injection of sclerosing agents into esophageal varices has satisfactorily controlled bleeding in some instances (17), but this procedure does not reduce the portal pressure. Frequent injections are usually necessary, and this requires repeated esophagoscopy examinations. It is probable that the varices will re-form as long as the high portal pressure exists. Furthermore, varices may be present in the stomach, and these cannot be attacked by this approach. This mode of treatment may be useful, however, as a palliative procedure in those patients upon whom operation cannot be performed.

Crile (18) has recently described the transesophageal ligation of bleeding esophageal varices, reporting a group of 7 cases. The follow-up period is short, and, again as in all methods which directly attack the esophageal vessels, no reduction in portal pressure occurs. There is every reason to believe that the varices will re-form. It does not seem logical that every vein in the involved region can be permanently obliterated.

Esophagogastric resection has been performed in the treatment of bleeding esophageal varices (19), but the cases have been few, the follow-up period short,

and the results inconclusive. The risk involved in these procedures is great, and it seems probable that new varicosities will develop in the remaining portions of esophagus and stomach if the portal hypertension still exists. Another investigator (20) has performed extensive gastric resection for esophageal varices, postulating that gastric anacidity is a protection against hemorrhage. It is assumed that bleeding from varices may be caused by peptic erosion of the esophageal mucosa. It is further contended that by removing the stomach, there is a significant decrease in portal blood flow, which should theoretically reduce the portal pressure. The mortality in this small group was 50 per cent and the follow-up period brief.

Som and Garlock (21) have recently described a procedure whereby the peri-esophageal region is packed with gauze in an attempt to promote the formation of granulation tissue and the subsequent development of collateral vessels between the esophageal and deep mediastinal veins. It would be worthwhile to record the portal pressure before and after this operation in order to establish whether any decrease occurs. The Talma-Morrison omentopexy has been employed sporadically for years in an attempt to establish new collateral connections between the portal and systemic veins, but at present it has largely been abandoned.

The procedure which has given the most promising results thus far in the treatment of portal hypertension has been the portal-systemic shunt. The rationale is logical: It is based upon the great pressure differential between these two systems. The pressure within the portal vein may be as high as 500 to 600 mm. of water, and that within the inferior vena cava and renal vein approximately 130 mm. After a successful anastomosis, there is a marked drop in pressure within the portal system. Reductions in portal pressure, ranging from 150 to 250 mm. of water are not uncommon. It is true that venous anastomoses generally tend to thrombose, but the marked pressure differential in these cases acts to keep the shunts patent. Vitallium tubes are often suitable for arterial anastomoses because of the high intraluminal pressure which maintains their patency, but they have been generally abandoned in the creation of venous shunts.

Practically every branch of the portal system has been joined to the inferior vena cava or one of its tributaries in an effort to reduce the portal pressure, but it is generally conceded today that the splenorenal and portacaval anastomoses are preferred because of the larger volume of blood diverted and because these large shunts have a better chance of remaining patent. Another technical advance has been the utilization of the combined thoracoabdominal approach, which affords vastly superior exposure at the operation. This incision has greatly facilitated the performance of these shunts, especially on the right side where the common duct and hepatic artery formerly proved so troublesome during the dissection of the portal vein.

During the past few years there has been some question as to whether the splenorenal or the portacaval shunt is preferable. The advantage of the splenorenal anastomosis is that it can be applied in practically all cases of portal hypertension since it is performed at the periphery of the portal system. Thus, it is applicable in all cases of hepatic or extrahepatic obstruction. In

those patients with a Banti's syndrome or other types of extrahepatic block, the portal vein is usually the site of pathology and is therefore unsuitable for a shunt. It is rare that the splenic vein is thrombosed or diseased to the point where it cannot be used for an anastomosis.

It has been recommended (11) that patients with a large spleen, esophageal varices, portal hypertension and the picture of hypersplenism should have a splenectomy and splenorenal anastomosis, but following a portacaval shunt the portal pressure is more effectively reduced and there is a corresponding decrease in the size of the spleen. Since the splenic vein in many instances is the only vein which can be utilized for an effective shunt, splenectomy alone should not be performed since it is invariably followed by thrombosis of the splenic vein. The removal of the spleen has the theoretical advantage of decreasing the total circulating portal blood flow by 20 to 40 per cent, but this procedure alone has not given satisfactory relief from portal hypertension. A two stage operation has been suggested (22) in the poor risk patient. The first stage consists of interruption of the splenic artery: This is followed by splenectomy and a splenorenal shunt as soon as the patient's condition improves. The universally accepted technic today in performing this operation is to anastomose the end of the splenic vein to the side of the renal vein, leaving the kidney intact (Fig. 2).

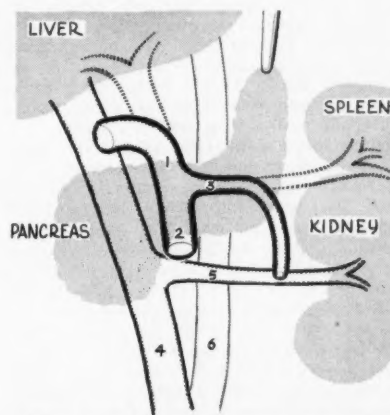


Figure 2: Schematic illustration of the portacaval and splenorenal anastomoses. 1. Portal vein; 2. superior mesenteric vein; 3. splenic vein; 4. inferior vena cava; 5. renal vein; 6. aorta.

The portacaval shunt, Figure 2, has its greatest field of usefulness in patients with cirrhosis of the liver. It allows for a greater drop in pressure than the splenorenal anastomosis. As stressed by Blakemore (23), the portal vein is larger and huskier than the splenic vein and is much easier to manipulate and suture. Arteriosclerotic changes are more frequently found in the splenic vein, especially in its distal portion, and there is also a greater chance of a twist occurring when this vessel is used for the anastomosis. The splenic vein has many more branches in the operative field and because of its close proximity to the pancreas, many hemo-

static sutures are necessary in order to control bleeding: The resultant inflammatory reaction may have deleterious effects upon the anastomosis. Finally, the splenorenal shunt usually requires more operating time and transfusions because of the more extensive dissection involved.

If it is feasible technically, it is preferable to create a portacaval anastomosis, but there are several difficulties inherent in this operation. One problem is the close proximity of such vital structures as the common bile duct and hepatic artery. By using the thoracoabdominal approach, these two structures usually fall away from the portal vein. Another difficulty is that the portal vein itself may be diseased and unsuitable for a shunt. There is often marked vascularity in the retroperitoneal region adjacent to the portal vein, and the resultant bleeding is sometimes difficult to control. Another theoretical disadvantage of the portacaval shunt is that the blood flow in the portal vein is completely diverted because an end to side anastomosis is usually performed. A side to side shunt would be ideal since the blood could flow in either channel and portal blood would continue to course through the liver. However, in many cases, it is technically impossible to approximate these two vessels either because of the distance which separates them or because the caudate lobe of the liver intervenes.

In a normal patient, sudden occlusion of the portal vein usually causes death. In a patient with portal hypertension, the portal system has been partially obstructed over a long period and the complete occlusion causes no apparent adverse effects. Following operation, there is usually a brief slight depression of liver function, but this usually returns to the preoperative level within one to two weeks. It is known that patients with extrahepatic obstructions, with practically all of the blood diverted from the portal vein, have usually completely normal liver function. The hepatic artery apparently takes over the burden of conducting blood to the liver.

Anticoagulants are not indicated in the postoperative period when a portacaval shunt has been performed because of the large size of the anastomosis and the marked pressure differential which exists. It is still a matter of dispute whether anticoagulants are necessary after creating a splenorenal anastomosis. Since the splenic vein is smaller than the portal, the anastomosis has a greater tendency to thrombose. It is difficult to visualize the patency of these portal-systemic shunts because the direction of flow is from the portal to the systemic vessel, and it is impracticable to inject contrast media into the portal system in order to visualize the anastomosis. It is therefore difficult to determine accurately what percentage of splenorenal shunts remain patent and whether anticoagulants are necessary.

THE SELECTION OF PATIENTS FOR OPERATION

One of the most important factors in the treatment of portal hypertension is the proper selection of patients for operation. It has been observed that less favorable results are achieved in those patients with ascites. It is advisable to postpone operation until the ascites has been eliminated by means of medical treatment. Patients with cirrhosis are poorer operative risks

generally than those with extrahepatic obstruction because of the impaired liver function. Very low mortality rates can be anticipated in the latter group because it usually includes younger individuals with normal liver function. However, even in those patients with liver disease, if the liver is fairly well compensated, a satisfactory outcome can be anticipated. Two valuable guides as to the optimum time for surgery are the serum albumin and the bromsulfalein test (24). If the albumin is 3 per cent or greater, and the bromsulfalein retention less than 30 per cent, the patient is usually a satisfactory operative risk. There are no hard and fast rules, however, and the complete clinical picture has to be carefully evaluated. The greatest possible improvement should be achieved preoperatively by means of vigorous medical therapy.

A difficult problem is that posed by the post-splenectomy bleeder. If the portal block is intrahepatic, a portacaval shunt is indicated. If the block is extrahepatic, the portal vein is usually unsatisfactory and the splenic vein is usually thrombosed as a result of the splenectomy. These patients are usually explored in an attempt to find a large portal tributary which can be anastomosed to a systemic vessel, but these shunts are usually too small to provide for a satisfactory drop in portal pressure. The difficulty in many instances is that even if a large portal branch is found, it is impossible to approximate it to a systemic vein. At the present time, vein grafts are being used in an attempt to overcome this difficulty: They should also prove useful in the performance of side to side portal vein to vena cava shunts.

Sporadic reports concerning the treatment of portal hypertension continue to appear, and a variety of surgical procedures are constantly being proposed. No matter what operation is performed, if it does not reduce the portal pressure, there is every reason to believe that bleeding will recur from adjacent veins. It is not conceivable that every vein in a given area can be completely and permanently extirpated by means of local procedures. Unless the patients are observed for long periods, it is impossible to evaluate any procedure. It is not uncommon for a spontaneous temporary cessation of bleeding from esophageal varices to occur. It is true that the portal-systemic shunt is technically difficult, and that it requires meticulous surgery, but it is the one procedure which has a sound rationale. If the pressure in the portal system is reduced, it is reasonable to assume that there will be less tendency for esophageal varices to bleed. It is true that the portal hypertension is secondary to liver disease in many of these patients, and that there is not a complete restitution of the individual to a normal status. However, if death due to bleeding esophageal varices can be averted, another opportunity becomes available for further liver regeneration.

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IN SITU HYDROGEN ION MEASUREMENTS OF THE MOUTH, ESOPHAGUS AND STOMACH IN NEWBORN INFANTS

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METHODS AND MATERIALS

THE HYDROGEN ion concentration of saliva and gastric juice in infants has been determined following collection of the respective fluids. Thomson (1) collected saliva by the capillary method in newborn infants, recorded the hydrogen ion concentration of the fluid and concluded that there is an increase in acidity from day to day for the first seven days of life. Huhtikangas (2) measured the gastric acidity by withdrawal of gastric contents of twenty-five fasting infants during the first fifteen minutes following birth. Subsequently, the same investigator made similar observations upon 260 fasting infants between five and twenty-four hours following birth.

Methods, other than extraction of fluids, have been utilized to obtain information regarding hydrogen ion concentration. In situ silver-silver chloride glass electrodes (3) have been used to determine hydrogen ion concentration of the nasal mucosa and nasal secretions in infants. The hydrogen ion concentration of the gastric juice in adults has been determined intragastrically with a glass electrode and recorded on a "Rohrenvoltmeter" (4). To the best of our knowledge, hydrogen ion concentration of the mouth, esophagus and stomach in infants has not been recorded through the use of in situ glass electrodes. The purpose of this paper is to report hydrogen ion concentrations of the mouth, esophagus and stomach in infants during the first forty-eight hours of life as determined by a glass electrode placed in an in situ position.

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The patients selected for this study were full term, normal infants born on the obstetrical service in the University Hospital. All observations were made on fasting subjects. The age of the infants ranged from three hours to forty-eight hours of age. There were twenty-six male and sixteen female infants, twenty-four of whom were negro and eighteen of whom were white infants. All recordings were made on a Beckman Model "G" Potentiometer. The potentiometer was adjusted to a pH of 7.4 by means of a known buffer. Temperature adjustment was maintained at 37.5°C throughout the study. The skin of the axilla was prepared with potassium chloride and a calomel sleeve electrode placed in the axilla. A glass electrode, measuring three mm. in diameter with an overall length of 1.27 cm. and attached to an insulated lead of 152.4 cm., was placed in the desired position. Except in the mouth, the electrode was placed in all other positions under constant fluoroscopic inspection. The glass electrode was placed under the anterolateral aspect of the tongue. This observation site is reported as mouth. Esophageal placement was immediately proximal to the "cardiac sphincter," and the readings are reported as esophagus. In the stomach, the electrode was placed in approximately the midportion of the fundus on the greater curvature. After recording the value at this point, the electrode was placed in the midportion of the pyloric antrum. Rotation of the infant to the right was necessary in some to obtain antral placement. A total of forty-two infants was studied. The

TABLE 1

Class—Mouth				Class—Esophagus			
24 hr. & under		24-48 hr.		24 hr. & under		24-48 hr.	
Series Obs.	(Obs) ²	Series Obs.	(Obs) ²	Series Obs.	(Obs) ²	Series Obs.	(Obs) ²
6.96	48.4416	6.03	36.3609	7.25	52.5625	6.81	46.3761
7.13	50.8369	6.63	43.9569	4.63	21.4369	6.78	45.9684
7.32	53.5824	6.75	45.5625	6.54	42.7716	6.21	38.5641
6.60	43.5600	6.54	42.7716	4.01	16.0801	4.79	22.9441
6.91	47.7481	6.59	43.4281	6.82	46.5124	6.64	44.0896
7.27	52.8529	6.32	39.9425	7.11	50.5521	6.54	42.7716
7.34	53.8756	5.57	31.0249	6.62	43.8244	5.40	29.1600
6.91	47.7481	6.99	48.8601	7.30	53.2900	6.72	45.1584
6.68	44.6224	6.50	42.2500	7.04	49.5616	5.23	27.3529
6.78	45.9684	6.68	44.6224	7.22	52.1284	6.69	44.7561
7.32	53.5824	5.73	32.8329	6.65	44.2225	5.25	27.5625
6.23	38.8129	6.95	48.3025	4.67	21.8089	6.73	45.2929
7.72	59.5984	6.47	41.8609	6.95	48.3025	5.36	28.7296
7.06	49.8436	6.20	38.4400	7.20	51.8400	6.40	40.9600
6.62	43.8244	6.30	39.6900	6.19	38.3161	6.40	40.9600
6.63	43.9569	5.43	29.4849	6.64	44.0896	6.68	44.6224
7.27	52.8529	6.25	39.0625	7.15	51.1225	7.03	49.4209
6.99	48.8601	6.38	40.7044	7.47	55.8009	6.52	42.5104
7.25	52.5625	6.04	36.4816	7.65	58.5225	6.29	39.5641
6.15	37.8225	6.08	36.9664	7.26	52.7076	6.75	45.5625
20)139.14	20)965.953	6.49	42.1201	20)132.37	20)895.456	6.49	42.1209
Mean 6.957	48.298	7.36	54.1696	Mean 6.6185	44.773	7.06	49.8436
		22)140.280	22)898.898			22)158.77	22)884.292
		Mean 6.376	40.859			Mean 6.307	40.195
Mean—6.96		Mean—6.38		Mean—6.62		Mean—6.31	
Range—6.15-7.72		Range—5.43-7.36		Range—4.01-7.65		Range—4.79-7.06	
Number—20		Number—22		Number—20		Number—22	
Corrected— .390		Corrected— .404		Corrected— .998		Corrected— .630	

observations were divided into two groups. In the first group were placed those infants under twenty-four hours of age, and in the other, those from twenty-four to forty-eight hours of age. Observations of hydrogen ion concentrations in the fundus and antrum were omitted in one infant because of vomiting during the course of the recordings.

OBSERVATIONS

The results of our observations are reported in Tables 1 and 2.

DISCUSSION

The observations of the hydrogen ion concentrations determined by us with the in situ glass electrode in

TABLE 2

Class—Stomach Fundus				Class—Pyloric Antrum			
24 hr. & under		24-48 hr.		24 hr. & under		24-48 hr.	
Series Obs.	(Obs) ²	Series Obs.	(Obs) ²	Series Obs.	(Obs) ²	Series Obs.	(Obs) ²
2.61	6.8121	2.22	4.9284	3.06	9.3636	3.19	10.1761
2.55	6.5025	1.82	3.3124	4.89	23.9121	3.42	11.6964
2.18	4.7524	1.82	3.3124	3.61	13.0321	3.38	11.4244
1.63	2.6564	1.73	2.9929	4.60	21.1600	5.13	26.3169
1.57	2.4649	1.61	2.5921	5.48	30.0304	3.06	9.3636
1.84	3.3856	1.82	3.3124	2.54	6.4516	4.85	23.5225
2.50	6.2500	1.73	2.9929	4.50	20.2500	3.24	10.4976
1.98	3.9204	2.34	5.4756	2.32	5.3824	3.01	9.0601
2.47	6.1009	2.35	5.5225	2.80	7.8400	2.80	7.8400
2.32	5.3824	2.32	5.3824	4.28	18.3184	2.55	6.5025
1.60	2.5600	1.19	1.4161	5.79	33.5241	4.21	17.7241
1.84	3.3856	1.62	2.6244	6.72	45.1484	5.63	31.6969
1.69	2.8561	2.72	7.3984	4.50	20.2500	6.45	41.6025
2.03	4.1209	2.50	6.2500	4.20	17.6400	3.80	14.4400
2.03	4.1209	1.85	3.4225	4.22	17.8084	3.70	13.6900
2.00	4.0000	2.29	5.2441	3.18	10.1124	3.31	10.9561
2.64	6.9696	1.87	3.4969	3.92	15.3664	4.46	19.8916
2.00	4.0000	2.00	4.0000	3.73	13.9129	3.79	14.3641
2.45	6.0025	1.82	3.3124	4.01	16.0801	4.42	19.5364
19)39.93	19)85.2437	2.19	4.7961	19)78.35	19)345.581	4.49	20.1601
Mean 2.101	4.4865	2.68	7.1824	Mean 4.123	18.188	5.63	31.6969
		2.15	4.6225			3.95	15.6025
		22)44.64	22)93.5898			22)88.43	22)377.610
		Mean 2.029	4.25408			Mean 4.019	17.164
Mean—2.10		Mean—2.03		Mean—6.62		Mean—6.31	
Range—1.57-2.64		Range—1.19-2.72		Range—4.01-7.65		Range—4.79-7.06	
Number—19		Number—22		Number—20		Number—22	
Corrected— .901		Corrected— .374		Corrected— .998		Corrected— .630	

the mouth are essentially in accord with the results of Thomson who used the capillary extraction method. This worker obtained a mean hydrogen ion value of 6.5 in the first twenty-four hours of life and a mean value of 6.04 in the second twenty-four hours. The mean obtained by us was 6.9 and 6.3 respectively on the first and second day of life. We are unable to compare the esophageal values of 6.6 and 6.3 in the first and second twenty-four hours of life respectively because there are no known results with which we can compare them. There exists considerable discrepancy between the hydrogen ion concentration of gastric contents in infants as obtained by the method of Huhtikangas and those values obtained through the in situ glass electrode method. Huhtikangas, in his study of fasting infants during the first fifteen minutes following birth, found the pH of gastric contents to range from 3.15 to 8.33. These values may have been influenced by whether or not amniotic fluid had been swallowed. Observations by the same worker on the 260 infants between five and twenty-four hours following birth showed the mean hydrogen ion concentration of gastric contents to be 1.45. The mean pH of the fundus, as determined by us, was 2.1 in the first twenty-four hours of life, whereas, the mean antral value during the same period was 4.1. It is recognized, of course, that we were measuring the hydrogen ion concentration of secretion covering the gastric mucosa; hence, comparison of the results by the two methods is not analogous. The observations in this study of an increasing hydrogen ion concentration in the second twenty-four hour period may lend support to the observation of Gilman and Cogwill (5). These workers noted that dehydration, experimentally produced in the animal, is accompanied by an increase in gastric acidity. The infants in this study did not receive any fluids until after forty-eight hours of life; hence, they can be termed dehydrated.

The significance of the recorded observations of this study is not apparent at this writing. That they might be related to smooth muscle motility might be inferred since it has been well-established that altera-

tions in hydrogen ion concentration alters the motility of smooth muscle (6, 7). Further, the lower numerical hydrogen ion value occurred in the fundus where peristaltic activity as observed under the fluoroscope was definitely slower than in the antrum where the hydrogen ion value was twice as great. Speculation might also be made as to whether the hydrogen ion value is a part of the enzymatic digestive action in the various areas. We did not in this preliminary study make any attempt to correlate hydrogen ion value with smooth muscle motility or enzymatic activity.

SUMMARY

Results are reported of the in situ mouth, esophageal and gastric hydrogen ion value in forty-two normal, full term infants, ranging in age from three to forty-eight hours of age. These results were obtained by a specially constructed glass electrode. Correlation of the results to other gastric functions was not attempted.

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BENTYL HYDROCHLORIDE SUCCESSFUL ADMINISTRATION OF A PARASYMPATHOLYTIC ANTISPASMODIC IN GLAUCOMA PATIENTS

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THE INTRAOCULAR pressure of the normal eye is said to be unchanged by atropine (1, 2) yet it is recognized that when there is a tendency toward increased intraocular pressure, mydriatics may augment it considerably (3). This is apparently the indirect result of dilation of the pupil, by which the lymph outflow is obstructed (1). Atropine, therefore, is contraindicated in cases of glaucoma and may represent a hazard

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*Bentyl Hydrochloride is the trademark of The Wm. S. Merrell Company of Cincinnati, Ohio for its brand of dicyclaniline hydrochloride (diethylaminocarbethoxydichlohexyl hydrochloride).

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in precipitating an attack of glaucoma when mild increases in intraocular pressure are not suspected and atropine or belladonna is administered.

Bentyl* Hydrochloride is a new, synthetic, parasympatholytic agent used in the treatment of functional bowel disease, peptic ulcer, and other gastrointestinal conditions associated with smooth muscle spasm. Pharmacologic studies (4) indicated a surprising degree of atropine-like action. Induced smooth muscle spasm could be restored to a normal motility pattern without producing the usual side effects of atropine, such as mydriasis.

It is of clinical interest that two cases of glaucoma

have been treated with Bentyt without apparent untoward effects.

Two female patients, one aged 69 and the other aged 70, both suffering from glaucoma and also from the irritable colon syndrome have been given oral Bentyt in dosage of 10 mg. four times daily for periods of 2 to 4 weeks at a time. Intermittent Bentyt therapy has been continued for over one year in each case without producing dilatation of the pupil or an increase in the intraocular pressure. Both patients originally required 2 per cent pilocarpine but are now maintained in 1 per cent pilocarpine. Local pilocarpine has not interfered with the antispasmodic effect of Bentyt upon gastrointestinal motility and there has been no evidence that Bentyt has inhibited the therapeutic efficacy of the pilocarpine.

In the case of one patient the intraocular tension, as controlled by pilocarpine, was 36 mm. of mercury before Bentyt therapy. After one year on Bentyt the tension was 30. In the second case, the comparable tensions were 30 mg. of mercury on pilocarpine before Bentyt; 28 mg. a year later.

COMMENT

It should be recognized that the clinical course of glaucoma is so variable that it is dangerous to predict upon only two cases seen personally and one other similar case as yet unreported by Chamberlin (5) that in no case will the intraocular pressure be influenced by Bentyt.

The author has treated over 300 cases with Bentyt and its compound, Kolantyl* of which 100 have been reported elsewhere (6, 7). These were all adults, suffering from a variety of organic and functional gastrointestinal diseases. Other investigators have reported 127 children (8) and 845 adults (5, 9-14), representing a total of 1,272 consecutive reported cases in which Bentyt was given without producing any mydriatic effect. Although the usual clinical dose that produces symptomatic relief in the vast majority of cases is 10 mg. to 20 mg., McHardy (9) employed 50 mg. doses in 266 consecutive cases and Hock (10) administered maximal doses of 130 mg. three times daily. Neither of these investigators observed dilatation of the pupil.

*Kolantyl is the trademark of The Wm. S. Merrell Company of Cincinnati, Ohio, for its brand of dicyclomine compound. Each tablet contains 5 mg. dicyclomine, 400 mg. aluminum hydroxide, 200 mg. magnesium oxide, 25 mg. sodium lauryl sulfate, and 100 mg. methylcellulose.

SUMMARY

Three patients known to suffer from glaucoma before Bentyt therapy apparently were free from altered intraocular pressure. Bentyt Hydrochloride is a new anticholinergic drug with a high degree of specificity for the gastrointestinal tract. In a series of 1,272 consecutive reported cases, including those receiving doses as high as 13 times the usual oral clinical dose, there has been no mydriatic effect.

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PRE- AND POST-SURGICAL USE OF INTRAVENOUS GLUCOSE INFUSION WITH AQUEOUS MULTI-VITAMIN COMPLEMENT: REPORT OF 137 CASES

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NUTRITIONAL deficiencies have always been a problem to the surgeon, particularly in emergency operations when little time is available to build up the nutritional status of the patient. Pre- and post-operative use of glucose infusions intravenously have proven universally of great value. Glucose alone, however, has not always proven adequate in a patient in a relatively poor state of nutrition, to overcome operative shock. Vitamin deficiencies have been known at times to be responsible, both directly and indirectly, in preventing healing or reducing the rate of healing after surgery.

Clark and Rossiter (1) report that conditions of shock and stress cause depletion of the ascorbic acid content of the plasma. McLester (2) quotes Lund as emphasizing the need of supplementary intravenous nutrition to alleviate previously existing or rapidly developing deficiencies.

Darrow and Pratt (3) recommend parenteral feeding of glucose with other nutrients including vitamins in the treatment of shock resulting from severe burns.

Among the nutritive elements known to have a striking influence on resistance to infections and phagocytosis and stimulation of healing are several of the B vitamins including riboflavin, pyridoxine, pantothenic acid, niacinamide, ascorbic acid, and the fat soluble vitamins A and D (4, 5, 6, 7). More recently, Chute (8) has indicated the need for replenishment of nutritional deficiencies by oral or parenteral means in pre- and post-operative surgery of aged patients.

The addition of the water-soluble vitamins to glucose solutions in post-operative surgery for intravenous infusion has become routine in many hospitals.

The advent of a more complete solution including the normally fat-soluble vitamins A, D and E in an aqueous medium (9) prompted us to try the addition of such a solution to glucose for intravenous infusions. This aqueous multi-vitamin preparation, Vi-Syneral Injectable (Intravenous)* in the form of a 10 cc ampule contains per ampule the following vitamins:

Vitamin A	10,000 units (U.S.P.)
Vitamin D (Calciferol)	1,000 units (U.S.P.)
dl-Alpha Tocopherol	5 mg.
Ascorbic acid	500 mg.
Thiamine-HCl	50 mg.
Riboflavin	10 mg.
Niacinamide	100 mg.
Pyridoxine-HCl	15 mg.
Panthenol (Pantothenic Acid equivalent)	25 mg.
Sorethyan Ester	1.0%
Stabilizing and preservative agents	2.0%

Submitted March 5, 1952.

*Vi-Syneral Injectable (I. V.) 10cc ampules supplied through courtesy of U.S. Vitamin Corporation of New York.

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This study was made in connection with 137 surgical patients, both male and female, varying in age from 15 to 72 years; 42 were males and 95 females.

Routine pre- and post-operative blood and urine examinations were made in each case. The procedure was relatively simple. Each patient was given an infusion of 1000 cc of 5% glucose solution to which was added the contents of a 10cc ampule of Vi-Syneral Injectable (I.V.). The infusion was given during the usual period of approximately one hour.

Detailed reports of the diagnosis and treatment of seven of the 137 cases follow:

CASE NO. 1—Mrs. E. S., age 36.

Diagnosis—Acute appendix, white cell count 20,000 per cu. cm. All other symptoms of acute appendicitis present. Operated and removed acute gangrenous appendix. Immediately after surgery, patient was given 1,000 cc. of 5% glucose with 10 cc. of Vi-Syneral Injectable intravenously. This was repeated on the second day post-operatively. There was no nausea or distension. Patient was able to tolerate fluids by mouth 6 hours after coming out of anesthesia. Uneventful recovery.

Urine pre- and post-operatively after the administration of Vi-Syneral (20 cc. in all) was negative.

CASE NO. 2—Mrs. M. D., age 36.

Diagnosis—fibroids. As an infant 4 months of age, this patient was operated on for the removal of a pyogenic kidney. Surgical procedure—hysterectomy, salpingectomy. This patient had had chronic pelvic inflammatory disease as evidenced by the fact that there were marked adhesive changes throughout the entire pelvic region.

This patient received 2 separate doses of Vi-Syneral Injectable 10 cc. in 1,000 cc. of 5% glucose and made a very uneventful recovery.

There was no evidence of post-operative shock, but the post-operative urine showed a 1 plus albumin—10 to 12 pus cells per high powered field and a few red blood cells. An examination of the urine one month later was normal.

This case is reported purposely because it is the only one of 137 cases which had any post-operative urinary complication and it is the feeling of the writers that this condition would have occurred had she received no vitamins intravenously, especially in view of the fact that this patient had only one remaining kidney.

CASE NO. 3—Miss V. M., age 46.

Diagnosis—Uterine fibroids. Surgical procedure, hysterectomy. Findings on the operating table were essentially the same as Case No. 2. Post-operatively, patient had 1,000 cc. of 5% glucose with 10 cc. of

Vi-Syneral Injectable intravenously. Recovery was uneventful. Discharged in 8 days. Urine pre- and post-operatively was negative.

CASE No 4—Mrs. Y. S., age 39.

Diagnosis—pregnancy (Primipara) with complications of uterine dystocia and cervical fibrosis. This patient was in labor 86 hours. During the process of labor, patient was given 2 doses of 1,000 cc. of 5% glucose with 10 cc. of Vi-Syneral Injectable intravenously for supportive measures, and at the end of the 86 hours of labor, it was decided with consultation to remove patient to operating room and manually dilate the cervix under general anesthesia and high forceps applied. This procedure took 3 hours. Patient left the delivery room in only fair condition and she was immediately given a 3rd dose of 1,000 cc. of 5% glucose with 10 cc. of Vi-Syneral Injectable intravenously. She made a very uneventful post-partum recovery. She was out of bed on the 3rd day after delivery. Post-partum urinalysis was negative. She was discharged on the 5th day after delivery in good condition.

CASE No. 5—Miss S., age 38.

Diagnosis—Allergic dermatitis of the hands and legs. This condition began 3 months prior to her admission to the hospital. On her own initiative, thinking she had a food allergy, she began to eliminate many of her nutritious foods, mainly proteins. She was admitted to the hospital with acute upper abdominal pains, nausea and vomiting and dehydrated, with increasing intensity of her rash. She was immediately given 1,000 cc. of 5% glucose with 10 cc. of Vi-Syneral Injectable intravenously. Nausea and vomiting stopped in 4 hours. A second dose of 1,000 cc. of 5% glucose with 10 cc. of Vi-Syneral Injectable intravenously was given on the following day and the rash began to clear up and was cleared entirely in one week. Urinalysis on discharge was negative. Diagnosis on discharge was multiple vitamin deficiency.

CASE No. 6—Mrs. K. V., age 41.

Diagnosis—Laceration of the vagina (3rd degree) following childbirth 16 months prior to operation. When first seen March 25, 1948, patient complained of loose stools, marked irritation of the vagina and rectum and occasional rectal hemorrhages. Examination at that time revealed a laceration of the vagina through the sphincter muscle and the mucous membrane of the rectum which converted the rectum and vagina into one common opening. The very slightest handling of these tissues would cause capillary hemorrhage. She was treated in the usual antiseptic fashion for about 11 months. High doses of multiple vitamins by mouth and especially high doses of Vitamin C were given during this period. As soon as these infected tissues had properly regained their normal tone, extensive repair procedure was attempted. On February 18, 1949 she was operated on to reconstruct the rectum, the sphincter muscle, and to rebuild a posterior vaginal wall, which was successfully completed. The usual post-operative anti-septic measures were instituted, and on the first 2

days post-operatively she was given 1,000 cc. of 5% glucose with 10 cc. of Vi-Syneral Injectable intravenously, and thereafter daily intramuscular injections of Vi-Syneral Injectable* 2 cc. for healing purposes for one week. The patient healed completely with no complications. When last seen 4 months after the operation, her rectal and vaginal tissues were all normal. Pre- and post-operative urine was negative.

*Each 2 cc. ampul contains

Vitamin A (natural)	10,000 U.S.P. units
Vitamin D (calciferol)	1,000 U.S.P. units
Alpha Tocopherol (E)	2 mg.
Ascorbic Acid (C)	50 mg.
Thiamine Hcl (B ₁)	10 mg.
Riboflavin (B ₂)	1 mg.
Pyridoxine HCl (B ₆)	3 mg.
Niacinamide	20 mg.

in an aqueous solution containing 4% wt./vol. sorbitol ester. With 0.5% Chlorbutanol (Chloroform derivative) as preservative.

CASE No. 7—Mr. N. B., age 55.

Diagnosis—Incisional hernia. This patient was operated on 10 years ago for an indirect hernia. When examined in October, 1948, the patient showed a bulging at the lower angle of the previous operation scar. On November 2, 1948 he was re-operated on and it was found that the bladder had herniated through the fascia of the anterior abdominal wall which was repaired. This patient had a severe smoker's cough. To minimize the danger of post-anesthetic bronchial irritation, Vi-Syneral Injectable, for its vitamin A content was given intravenously, 1,000 cc. of 5% glucose with 10 cc. of Vi-Syneral Injectable, for 2 days. Patient made an uneventful recovery. Discharged in 2 weeks. Pre- and postoperative urinalysis was negative.

SUMMARY AND CONCLUSIONS

In the remaining 130 cases pre- and post-operative intravenous administration of Vi-Syneral Injectable in glucose failed to produce any toxic symptoms or untoward reactions.

1. 137 patients in all, under surgical observation and treatment, were given intravenous infusions of glucose with a complete aqueous multi-vitamin formula without any evident signs of toxicity or untoward reaction.

2. Routine Urine examination failed to reveal any difference between the pre- and post-operative examinations.

3. There was a definite decrease of the incidence of post-operative nausea and vomiting.

4. An increased feeling of well being was observed in the majority of patients and they appeared to look brighter and more alert within 24 hours after surgical procedure as compared to the non-vitamin treated patient.

5. Wound healing was stimulated beyond those previously seen before vitamin therapy was instituted intravenously.

6. The post-operative increase of appetite appeared to return sooner than usual. This apparently was due to less post-operative abdominal distention.

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ABSTRACTS ON NUTRITION

RIVAS, F. D., SUAREZ, R. M., MORALES, F. H. AND SANTIAGO, E. P.: *The oral administration of vitamin B₁₂ in tropical sprue*. Ann. Int. Med., 36, 2, Part 2, 583-590.

Vitamin B₁₂ alone, given by mouth, was found to have definite but limited hemopoietic value in sprue. Gastric juice potentiated the activity of B₁₂ orally in 2 out of 3 cases. Large single doses of B₁₂ (90 to 450 micrograms) orally failed to give a response in 3 out of 4 cases. Large daily doses of B₁₂ orally produced a slow, suboptimal response in 2 cases. It was found that the oral use of B₁₂ in sprue is not the most efficient or practical way to treat sprue. Fifteen mg. of folic acid by mouth, or 15 mcgm. of B₁₂ intramuscularly are much more effective. In sprue, the intestinal absorption of B₁₂ may well be impaired, even when intrinsic factor is present.

MARSHALL, W.: *Insulin dosage in diabetics: a simplified method of determining initial insulin dosage in diabetics*. Med. Times, 80, 3, March 1952, 167-168.

Marshall found that one unit of plain insulin will reduce the blood sugar by 3 mg. percent in 2 hours. In cases in coma, he subtracts 120 from the blood sugar reading, as 120 is taken as the upper limit of normal blood sugar. By dividing the remainder by 3, he obtains the number of units of insulin to be given to bring the blood sugar down to normal in a short time. He has found that the method works out well in practice.

FINEBERG, S. K. AND ALTSCHUL, A.: *The encephalopathy of hyperinsulinism*. Ann. Int. Med., 36, 2, Part 2, Feb. 1952, 536-550.

The thesis of this contribution is that the use of insulin may at times produce severe and permanent damage to the brain, with such symptoms as hemiparesis, ataxia, incontinence, aphasia, choreiform movements, Parkinsonism, epilepsy, mental deterioration or idiocy. As a rule, such results have followed the use of very large doses of insulin to combat acidosis and coma. Not infrequently death ensues despite fairly good regulation of the blood sugar level. In either case the main damage was found to be (as checked at autopsy) extensive alterations in the nuclei of the neurons, which in many instances were displaced, pyknotic and even frag-

mented. Such results obviously depend on a low brain sugar. There is no necessary correlation between blood sugar and brain sugar. An insufficiency of glucose in the blood may not, under some circumstances, produce an insufficiency of cerebral cellular content of glucose, and, conversely, a sufficient blood sugar may not always insure an adequate intracellular content. The brain cells are not always capable of taking up glucose and/or incapable of oxidizing glucose. In cases where such encephalopathy does not respond immediately to glucose, and there appears to be danger of permanent cerebral damage, the use of ACTH and adeno-cortical hormone is suggested.

BENSTEAD, N. AND THEOBALD, G. W.: *Iron and the "physiological" anemia of pregnancy*. Brit. Med. J., Feb. 23, 1952, 407-410.

Of the hemoglobin readings from 2,000 consecutive cases at or below the 16th week of pregnancy, 60 percent were subnormal and 6.5 percent showed severe anemia. This anemia is associated with a subnormal corpuscular hemoglobin concentration, but normal values may be maintained by the use of ferrous sulfate in therapeutic doses throughout pregnancy. Molybdenized iron is better tolerated but not more effective than ferrous sulfate.

CREGO, C. H.: *Vitamin-resistant rickets*. Mississippi Valley Med. J., 74, 2, Mar. 1952, 52-53.

Vitamin-resistant rickets is severe rickets which responds only to massive doses of vitamin D. The exact underlying metabolic error is not known but treatment is based on the threshold concept for each individual patient. The author believes the disease is a very common one, in the past wrongly classified and diagnosed, and represents the most common single cause of dwarfism (chondrodysplasia). Sufficient vitamin D must be given to raise the serum calcium to normal or slightly above, to increase the serum phosphorus, to decrease the alkaline phosphatase and to increase the urinary output of calcium to a 2-plus Sulkowitch reaction.

CLARK, G. E.: *Symptomatology of achlorhydria*. Texas State J. M., 48, 3, March 1952, 125-126.

Clark believes that achlorhydria, itself, may be responsible for such symptoms as gas, belching, epigastric

pain and pressure, diarrhea, nausea, epigastric burning, secondary anemia, as well as other symptoms such as "sour stomach," excessive flatus, pain in the right lower quadrant and constipation, largely because he has seen these symptoms disappear after the use of dilute HCl in 67 cases of achlorhydria in which other gastrointestinal disease was ruled out. He does not state the dosages employed. Using 2 ounces of 7 percent alcohol as a stimulant was his method of determining presence or absence of free HCl. Achlorhydria occurs in from 3 percent of persons in the third decade to 30 percent in the seventh and eighth decade.

ROLLAND, C. F.: *Diabetes mellitus in surgical patients*. Brit. Med. J., Apr. 5, 1952, 737-740.

Details are given of a series of 300 consecutive surgical diabetics, the majority being over 50 years of age. Gangrene of the foot was the most common single disorder. Forty-one of the patients were not known to be diabetic when admitted to the surgical wards. The overall mortality was 9.3 percent. Diabetic coma was unimportant as a cause of death. Diabetic ketosis is often complicated by symptoms suggesting the presence of an acute abdominal emergency, but these symptoms usually subside as the ketosis is corrected. Such cases present great diagnostic difficulty. When thirst, polyuria and drowsiness precede the abdominal symptoms, it is likely that the ketosis is responsible for the whole clinical picture, but when the symptoms appear in the reverse order, it is likely that the ketosis is the result of an acute abdominal emergency.

BEDFORD, P. D.: *Side-effects of a preparation of vitamin B₁₂*. Brit. Med. J., March 29, 1952, 690-691.

Of 100 people, 14 were skin-test-positive to a vitamin B₁₂ concentrate derived from *Streptomyces griseus*, and six suffered side-effects after intramuscular injection. Two were skin-test-positive to a purer preparation of vitamin B₁₂ derived by crystallization from streptomyces cultures, and none developed side reactions to intramuscular injections. None reacted adversely to a preparation of vitamin B derived from liver. Impurities carried over from the mould fermentation are regarded as responsible for the sensitivity phenomena. Both cutaneous reactions and side-effects were more than twice as common in persons who had previously been treated with antibiotics. The possibility of inducing idiosyncrasy to antibiotics is advanced against the use of impure preparations of vitamin B₁₂ derived from mould cultures.

JACKSON, W. P. U., AND LINDER, G. C. *Small gut insufficiency following intestinal surgery. I. A clinical and metabolic study of a man surviving with seven inches of small intestine*. South African J. Clin. Sci., 2, 1, Mar. 1951, 70-112.

This is an extremely thoughtful and detailed examination report of the metabolic and other aspects of a patient, Toni, who was left with 6 or 7 inches of small gut following an operation. The condition necessitating such drastic removal was a volvulus developing after a previous superior and mesenteric artery thrombosis, and accompanied by fresh thrombosis of the collateral vessels. Six months after the operation, Toni developed a pellagrinous state. Slight abnormali-

ties in behavior were noted, which culminated in epileptic fits and the beginning of a true fluctuating psychosis despite continued administration, parenterally, of the vitamin B group. Metabolic studies showed a large loss of protein, phosphate calcium and salt in the feces, and almost complete absence of fat absorption. The nitrogen balance was positive and the calcium balance was negative.

Absorption of carbohydrates and alcohol was almost complete. The production of the pancreatic and intestinal enzymes was feeble. Salt and water were retained temporarily in the body and excreted after a delay, usually at night. Dr. S. Berman who makes the psychiatric report believes his mental condition was certainly due to having lost so much small gut. His condition might be termed a "pellagrinous psychosis of mixed type," but actually it cannot be easily classified. Certainly his mental condition did not respond to thiamine or nicotinic acid. Possibly irreversible changes had occurred before such therapy was begun, or the psychosis might represent a failure of integration of the whole personality to the total life situation in which he found himself. (The case may be of importance in that it suggests that psychoses may sometimes have a basis of faulty nutrition.)

MELLANBY, SIR EDWARD: *Chemical manipulation of food*. Brit. M. J., Oct. 13, 1951, 863-869.

Both in Britain and the U.S.A., chemicals which are assumed to be harmless may be added to food and their harmful properties are only realized after a lapse of time. He cites the case of aminopyrine, long in use as a medicine, which was finally shown to produce agranulocytosis, and also resorcinol, long used in skin diseases, which is capable, in some people, of producing myxedema and thyroid enlargement. In regard to food, Mellanby admires the Food and Drug Administration in the U.S.A. and thinks Britain should have a similar Bureau. Food processing entails the danger of adding to food something which will prove toxic, and also the danger of reducing the nutritive value of food by the reduction of some of its important constituents. He makes an extended survey of chemicals used in food preparation and concludes that manipulation of food may in many instances produce "error in living" which requires investigation. If people want bread which has not been chemically treated in any way, Mellanby thinks it should be made available to them. Untreated flour should be freely available for home baking of bread.

MUKHERJEE, C.: *Plasma alkaline phosphatase in toxemia of pregnancy*. J. Indian Med. Assn. XXI, 2, Nov. 1951, 43-52.

Study of the plasma alkaline phosphatase in 93 cases of normal pregnancy indicates that during the last three months of pregnancy the phosphatase values are high according to the accepted standards. This abnormal level is probably due to the physiological demands of the fetus. Phosphatase in pre-eclampsia and eclampsia is abnormally high due to the hepatic dysfunction which accompanies toxemia of pregnancy. Phosphatase is high in accidental hemorrhage and shock but neither nephritis or compensated hypertension in pregnant women cause any elevation. Labor, especially prolonged labor, increases phosphatase levels even in normal women. During the first week of the puerperium the values start to return to normal.

EDITORIAL

IMMEDIATE AMBULATION

The swing of the pendulum toward early and immediate ambulation for surgical patients is now almost complete. The general surgeon and the proctologist who does not advocate early or immediate ambulation after surgery is rapidly becoming outdated.

The change in attitude is evidenced in the literature, and in most progressive hospitals. In 1949 one author wrote, "The patient may be discharged from the hospital between the second and fourth post-operative day after a bowel movement has occurred" (1). The same author stated, "Ambulatory operative therapy is usually incomplete in scope."

A report published by this author in 1952 indicates a reversal of attitude (2). "Simple proctological lesions, such as perianal hematomas, verrucae, short sinus tracts, etc., are treated ambulatorily either in the office or in the operating room without hospitalization by many proctologists and general surgeons." He further states, "the hospitalized patients are usually ambulated within 8 to 24 hours after operation and are discharged after the first active defecation which usually occurs in 36 to 72 hours."

It is good to note that even the most severe and articulate critics of early ambulation now advocate ambulation within 8 to 24 hours after operation and discharge from the hospital in 36 to 72 hours. It would be interesting, however, to know why a patient who is ambulatory 8 hours after surgery must sit around the hospital for an additional 28 to 64 hours. The answer may lie, of course, in the frequent need for morphine in these cases, and in the surprisingly high frequency of post-operative complications.

However, there would appear to be two other criticisms of immediate ambulation as employed by the proctologist. One, it is claimed that some who practice this technic perform incomplete operations. Two, it is stated that some of these patients remain bedridden at home for some time.

It has also been said, but undoubtedly in jest, that some of these patients have indicated they would not again submit themselves to anorectal surgery without hospitalization. This could not have been reported in any seriousness by the author, inasmuch as it would be difficult to find any patient who has had anorectal surgery performed either with or without hospitalization who would be happy to again submit himself to such surgery.

Indeed, the very author who reports this emotional reaction indicates that 80% of his hospitalized patients required morphine post-operatively. With the semi-closed type of hemorrhoidectomy considerably more morphine was required. Indeed, the post-operative course in about 20% of these cases was complicated by induration and tenderness in the wound. After a closed hemorrhoidectomy the post-operative course was said to be "quite stormy in some patients" and about 4 times more morphine was required than after

the open operation. Over 50% of these patients developed induration, tenderness, and in some cases localized suppuration requiring drainage. "A number of patients" also developed "relative anal stenosis." *These were all in hospitalized cases.* It would be interesting to know how many of these patients would like to be operated again in the hospital.

This is an interesting contrast with properly performed ambulatory proctologic technics. Surgery is exactly the same as for the hospitalized patient. *It is complete* (6). Complications, however, are relatively few, morphine is practically never required, and patients are back in relatively full activity (with rare exceptions) within one or two days after surgery. There is no doubt that there will be an occasional neurotic patient who prefers to remain in bed for an additional day or longer after surgery. These patients will be equally neurotic whether the surgery is performed in ambulatory fashion or in the hospital. However, there is less chance of developing psychosomatic complaints if early or immediate ambulation is practiced. In a discussion of the psychologic basis of early ambulation, Hardy states, "a respectable body of evidence supports the view that early ambulation hastens the total rehabilitation of the individual following injury" (3). The importance of the psychosomatic factors in convalescence are well recognized by this author.

He further states, "The psychologic reorientation of both the physician toward the patient and the patient toward himself has been a major accomplishment of early ambulation. When the patient is helped out of bed the day following what he thought was an operation which would inactivate him for a considerable period of time, he quickly begins to take a certain pride in his recuperative powers, and this pride flows under the skillful guidance of a thoughtful physician. Under such care the patient becomes increasingly extraverted rather than introverted, and many practical and tangible advantages are derived from such a program."

There can be no doubt that the patient on prolonged bed rest will often develop emotional problems. There can also be no doubt that the benefits of early or immediate ambulation are not to be considered a complete panacea for all post-operative ills. The patient who is neurotic before surgery will remain neurotic after surgery, whether hospitalized or ambulatory. Therefore, to criticize a technic because one or one hundred out of many thousands of cases is dissatisfied, (or stays in bed at home) is shortsighted, statistically unbalanced, and illogical. On this basis we would have to discard most of the technics of surgery and medicine. Results are far from 100% with any procedure.

The advantages of early ambulation have been recognized for a very long time. The history of this subject is well covered by another author (4). In proctology, as far back as 1942, Hirschman stated, "The majority of the diseases affecting the anorectal region are entirely amenable to surgical treatment under re-

gional anesthesia. The amount and extent of proctologic surgery performed by any one individual in office practice is necessarily limited to the ability and equipment of the individual. For economic, psychic, or other good reasons, it may be necessary to perform certain surgical procedures in one's office, and allow the patient to be taken to his home afterward. In the hands of the skilled proctologist whose office is especially equipped with adequate surgical, as well as recovery facilities and sufficient trained personnel in attendance, a large group of surgical procedures can be performed without hospitalization (5).

In 1946 my own text on ambulatory proctology, advocating immediate ambulation after proctologic surgery, first appeared (6). (The rapid swing of the pendulum toward early and immediate ambulation is further evidenced by the fact that this text is now in its second edition.)

As Hirschman has stated, the extent of the surgery to be performed by the individual operator depends upon his skill and ability, as well as his equipment. As has been demonstrated in many hundreds of cases, extensive fistulectomy, pilonidal cyst operations, rectal prolapse, internal and external hemorrhoids, etc., may be operated *completely*, under caudal analgesia, with ambulation 45 minutes after surgery. This is not to indicate that every surgeon is so equipped, either in skill or in physical armamentarium. Those who are not so equipped should not attempt to do extensive surgery to be followed by immediate ambulation. This is true whether the patient is operated upon in the office or in the hospital. *The nature and extent of the surgery should be the same whether or not the patient is hospitalized.*

There can be no doubt that there are some surgeons who operate in ambulatory fashion and do incomplete surgery. However, the same may be said of some surgeons who operate in hospitals. The difficulty does not lie within the concept but with the surgeon.

The advantages of immediate or early ambulation are numerous. The physiologic and anatomic rationale for early and immediate ambulation are now well established in the literature, and need not be repeated here (4). There is no doubt that the vast majority of these patients do better, physiologically and psychologically, than the patients who are kept in bed for a prolonged period of time, whether at home or in the hospital. The economic advantages are even more tremendous.

The cost of hospitalization is mounting so rapidly that the average patient who does not carry hospitalization insurance cannot afford to be hospitalized. Further, the loss of income while hospitalized is an important factor. Thus, physiologically, psychologically and economically the patient who is given the benefit of early or immediate ambulation is generally a happier person.

In summary, there is both precedent and increasing authority for the performance of rectal surgery in ambulatory fashion with the return of the patient to his home. Mounting costs of hospitalization have further increased the economic significance and importance of these technics.

It could not be that the staff position of some physicians depends upon the number of cases hospitalized. It could not be that the fee for surgery may be greater if the patient is hospitalized. Nor can it be that the problems of nursing and supplies, and large expenditures required to staff, equip and maintain the office of the operating ambulatory proctologist would deter any surgeon from employing these methods. There is no doubt that political and economic considerations such as these do not influence the reputable proctologist or surgeon. The need of the patient is the first consideration in the heart of every surgeon. Thus, there is no doubt that the pendulum will swing still further, and that early and immediate ambulation will become even more general than it is at present.

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BOOK REVIEWS

THE STORY OF THE ADAPTATION SYNDROME. Hans Seyle, M. D., Ph. D., D.Sc., F.R.C.S. 225 pages, Acta, Inc., 5465 Decarie Blvd., Montreal 29, Quebec, Canada, \$4.50.

Here, for the first time, Seyle tells the story of the general adaptation syndrome in simple narrative style, so that the reader may more clearly grasp its significance and also learn the history of this "great idea" as it took form in Seyle's mind. Beginning at first as an unwelcome but obligatory explanation of some frustrated experiments which he had done in connec-

tion with the sex hormones, it eventually became the only logical explanation of those solid facts which are now evident to everyone who has studied the experiments. The fact that laboratory animals reacted identically under the influence of injuries of the most diverse nature, and exhibited adreno-cortical enlargement, acute involution of the thymico-lymphatic apparatus and bleeding ulcers of the stomach and duodenum, was one which might easily have been overlooked by an orthodox investigator. It was certainly one which usually would have failed to initiate the long

and tedious combination of theory and experiment which, in Seyle's case, resulted in one of the most far-reaching generalizations in the history of medicine and physiology.

It is now unnecessary to repeat that injury, whether of a chemical, physical or psychic nature, if sufficiently strong, causes the sudden appearance of the phenomena mentioned and brings about the "alarm" reaction, which may prove rapidly fatal (shock), or, if submaximal and continued, produces a more-or-less prolonged period of "resistance," culminating in a period of "exhaustion," unless the injury is discontinued. Owing to Seyle's persistence in writing and in lecturing, the medical world today has a fairly good understanding of these important phenomena, and of the dominant role of the pituitary and suprarenal glands in their mediation. Ironically, the adaptation syndrome is best illustrated by those very instances in which adaptation fails, owing to a "derailment" of the natural chemical process of attempted resistance.

Today no one knows how far Seyle's work may go in explaining the fundamental nature of health and disease but the facts are now incontrovertible and the theories are as adequate as anyone has been able to furnish. The book is extremely interesting because of its informal approach and it is pre-eminent among the seven or eight volumes which have come from Seyle's pen, because of its simplified presentation. The initial periods of Seyle's researches,—some 16 years ago—form fascinating reading for several reasons. First, the story of his intellectual frustration upon first realizing that he had failed to prove what he set out to do is a common experience in the lives of all investigators. Second, when he was presented with the fact that injuries of the most diverse nature produce physiological and anatomical changes of an identical nature, he could easily have abandoned his researches as a *cul-de-sac* of the most pernicious type. It was at this point,—when his friends and superiors advised him to drop the entire subject—that Seyle's essential genius became manifest. One aspect of genius is the capacity to take an unorthodox viewpoint, and to suspect that what appears dross is actually gold.

His training as a physician had naturally inbred in him the habit of looking for *specific* causes. But in his experiments he was confronted with *specific results* and a long list of extremely nonspecific causes. The tables had completely turned. Seyle began to see that people get sick, not so much from specific causes, as

from the continued *stress* of almost any kind of physiological insult. He took heart and, with great inspiration, applied himself to an explanation of this most unorthodox idea.

Today, no one can reasonably criticize the factual findings Seyle has accumulated and, thus far, no one has come forward with a theory more convincing than his to explain these findings.

Seyle is an unusual combination of intellectual capacity, industry, and missionary zeal. He is not only a distinguished scientist but also the St. Paul of modern medicine. It is one thing to make an incisive physiological discovery, which has within it the potentiality of reshaping our entire medical thinking. It is perhaps even slightly more difficult to realize the importance of spreading the gospel, and then actually to spread it as Seyle capably does in this writing. It is the reviewer's belief that, while future investigation may alter Seyle's concept of the General Adaptation Syndrome, he has nevertheless brought forth the only idea within the past six decades which contains the power of eventually bringing about a fundamental revolution in medical thought. Collateral investigations in physiology and even in psychology have, within the past five years, strongly tended to emphasize and corroborate Seyle's conception of stress as the master cause of disease. It is therefore becoming more and more urgent to understand the endocrine adaptations to the various forms of stress and less important, though still pertinent, to study the exact nature of the stress itself.

THE TREATMENT OF ACUTE DEHYDRATION IN INFANTS, BY A WORKING TEAM APPOINTED AND ADVISED BY THE COMMITTEE ON ACUTE INFECTIONS IN INFANCY. Published by the Medical Research Council (Memorandum No. 26). Her Majesty's Stationery Office, London, (P.O. Box 569, S.E.1.), 3 shillings, 1952.

In about 50 pages, the Working Team, consisting of nine prominent medical authorities, has presented all that is necessary to know about the treatment of moderate or severe dehydration in infants, and the treatise consists rather in the orderly presentation of known methods than in the introduction of any new methods. Electrolyte balance and parenteral nutrition both receive extensive comment. The book is highly recommended to all physicians and surgeons.

GENERAL ABSTRACTS OF CURRENT LITERATURE

ALEXANDER, FAY K. "Duodenal ulcer in children." *Radiology* 56, 6, 799. June 1951.

Children can and do have duodenal ulcers. Conservative estimates put the incidence at about 1.5%—frequent enough to warrant consideration in diagnosis of recurrent abdominal pain associated with nausea and vomiting. In roentgenographic studies of the gastrointestinal tract of 254 children Alexander found 30 cases of duodenal ulcer. The patients were 2 to 14 years of age, 18 were boys.

Chief symptoms are abdominal pain, usually generalized but occasionally periumbilical or epigastric, nausea, and vomiting. Blood is sometimes seen in the vomitus and stool. The adult patient's symptom complex of pain, food, relief is not apparent in children. The abdominal pain is often considered due to mesenteric adenitis, food allergy, or gastroenteritis from dietary indiscretion. Sometimes appendectomy is performed unnecessarily. Nausea and vomiting are usually quite severe. During these attacks, anorexia usually causes loss of weight and constipation. Vomiting is of the type associated with pyloric spasm, since symptoms subside

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once the stomach has been emptied. Laboratory findings are usually not helpful, physical examination only occasionally elicits abdominal tenderness.

The uncomplicated ulcer seen in children is a shallow mucous erosion which involves only the mucosa, rarely extending to the submucosa. Since the muscular and peritoneal coats are not included in the inflammation, pain is not localized but is a diffuse gastric distress. Spasm of the pylorus and duodenum, frequently seen fluoroscopically, indicates disturbance of the intestinal gradient which is responsible for nausea and vomiting.

Symptoms alone do not establish the diagnosis. A niche defect must be demonstrated by roentgenograms.

Dr. Franz J. Lust.

RACHET, J., BUSSON, A., RODE, JACQUES, ROBIN-
EAU, ROGER: *A.C.T.H. and Cortisone in the treat-
ment of ulcerous recto-colitis.* (Paris, Hospital
Bichat) Arch. Mal. App. Digest. 40, 11. 1951.

After using Cortisone and ACTH during the last six months in the treatment of patients suffering from ulcerous recto-colitis, we are now able to report on ten cases; eight of these patients have been treated by Cortisone and two by ACTH. We intend to analyse the results obtained; to compare our findings with those on the same subject previously published abroad; to make clear our conclusions regarding a therapy which we consider as non-specific and in some cases, dangerous.

The patients with ulcerous colitis whom we have had to treat suffered from severe forms of the disease, either of recent or ancient date, and had not responded to the usual treatment. In several cases, X-ray examination showed the greater part of the colic intestine to be involved. All our patients were hospitalized and kept to a strict salt free diet for as long as the treatment lasted. Posology varied with each case; on the whole the total doses reached about 2.50 gr. The scheme of treatment most frequently adopted was the following:

Cortisone: 300 mg. the first day; 200 mg. the second day; 100 mg. the third day; then 100 mg. daily during the last days of treatment.

ACTH: Daily doses from 60 to 100 mg. during 15-20 days followed by decreasing doses. We soon found ourselves compelled to associate an antibiotic such as Aureomycin or Chloramphenicol to our treatment; and this, at the very onset of treatment. To judge the progress of the disease, the following were considered: Number and appearance of stools; Temperature, body weight, general condition, rectoscopy (repeated every 2 or 3 days). Laboratory investigations, including: Thorn's test, and absolute number of eosinophiles per mm³. Plasmatic chlorine and urinary chlorides. Alkali reserve, glycemia, blood sedimentation rate, blood sodium and blood potassium, electrocardiogram. Rate of urinary discharge of Aceto-steroïdes and N oxycto-steroïdes.

The number and appearance of stools were favorably influenced in only 4 cases out of 10. The action of treatment on temperature was the clearest and most constant symptomatic improvement. The action on the general condition of patients was unequal. For us, rectosigmoidoscopy remains the main element and is essential for judging the progress of any ulcerous

colitis. Repetition of this is not superfluous since certain authors have thought it possible to publish spectacular functional results obtained in the treatment of this disease by Cortisone, without giving any results of proctological examination. Unfortunately, none of our patients showed any favorable change in the endoscopic results: a slight and only transitory decrease in suppuration was observed in only three cases. We were never able to note the slightest improvement in congestive, hemorrhagical or ulcerous lesions. It seems to us that this complete absence of anatomical modifications means that neither Cortisone nor ACTH have any specific action on ulcerous colitis.

An incomplete Cushing's syndrome could be observed in two of our patients. With another patient, when a normally salted diet was allowed 8 days after the termination of the cortisone treatment, a sudden increase in weight and a malleolar edema were observed.

In one case a total colectomy was realized 4 days after the termination of a treatment by 1,200 mg. of cortisone; it was followed by torpid peritonitis. It must be noted that this local and general infection developed without fever in a patient who had not really recovered from post-operative shock. Death took place three days later in spite of intensive antibiotic therapy. We definitely considered cortisone responsible for such a complete absence of organic defense. If surgical treatment seems advisable, we consider it absolutely necessary to allow three weeks to elapse after the end of cortisone therapy. The coexistence of arthritis does not constitute a sufficient pathological reason to justify the use of cortisone in ulcerous colitis. Cortisone acts symptomatically on the arthritis but its action does not go any further. One of our cases confirms William Dearing's reports.

Neither cortisone nor ACTH constitute a specific therapy of ulcerous colitis. These hormones are practically without any effect on the local lesions of the disease. Moreover, these treatments involve real danger and necessitate special precautions. One can hardly hope to obtain more than an improvement of concomitant arthritis where it exists, and, in some cases, a general and functional improvement.

Guy Albot, M. D.

MOXO, D., AGUSTI, J., AND ROCA DE VIÑALS, R.: *Eosinophile infiltration of the stomach and pyloric hypertrophy in the adult.* Revista Española de Enfermedades del Aparato Digestivo Y de La Nutricion.—Num. 5, 1951.

The authors describe a case of pyloric hypertrophy with eosinophile infiltration diagnosed radiologically as a gastric neoplasm and in which the laboratory findings (histo-pathology of the specimen and a sternal puncture) demonstrated the true nature of the condition. The authors make the following considerations.

Pyloric hypertrophy of the Adult.—In medical practice, pyloric hypertrophy in the adult has not been properly evaluated, in spite of it being a well known entity in Pediatrics. Mayer, in 1888, was the first to describe this condition. Posteriorly, other cases were published by Mayo-Robson, Moynihan, Barling, Paul and Johnson, Rundstrom, etc.

The causes of pyloric hypertrophy are not known.

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Some authors maintain that the non-operated congenital cases may continue to present organic alterations, even after the disappearance of clinical symptoms. These organic changes may be the cause of digestive disturbances in adult life. Others believe in the theory that the prolonged pylorospasm is the cause of the hypertrophy of the sphincter. A third theory pretends to correlate this condition with an allergic basis produced by antigenous foods, and still others have proposed the hypothesis that the hypertrophy is due to a protein deficiency secondary to malnutrition.

The authors of this article believe that pyloric hypertrophy may persist asymptotically from infancy to become manifest sometime during adult life. The hypertrophy of the circular muscular coat is the characteristic anatomo-pathologic feature and does not continue beyond the pyloric ring; in the mucosa and the submucosa, one always finds foci of nonspecific cellular infiltrations.

Massive Local Eosinophile Infiltration.—It is not uncommon to find eosinophiles in certain chronic inflammations of the intestinal tract, but these are rare and form part of the typical leucocyte reactions of all the local inflammatory processes. Besides, in such cases, the mentioned elements may be found, with preference, in the submucosa and in the mucosa, while in the case presented by Dr. Moxo and Co-workers, the infiltration was truly eosinophile and was found exclusively between the bundles of hypertrophied muscular tissue of the pylorus, constituting a true and microscopic eosinophile granuloma, analogous to those published by Barrie and Anderson and by Spencer, etc.

Eosinophilia.—It was not possible to demonstrate in this case, the existence of eosinophiles in the peripheral blood. The authors believe that this is probably due to the fact that the patient was operated upon without having experienced any of the paroxysmal crises which the patient refers to in his clinical history; nevertheless, a study of the bone marrow revealed a clear central eosinophilia with 18 per cent of eosinophile granulocytes, thus proving the existence of a latent eosinophilia. The cases presented by Barrie and Spencer, showed peripheral eosinophilia only during the acute crises, with a descent to almost normal findings during the quiescent stages.

The authors believe that the case studied, corresponds to a Diathetic Hemodystrophy probably related to a constitutional disturbance with neurovegetative participation. This criterion is substantiated by the existence of the pyloric hypertrophy and the eosinophile infiltration.

Diego Moxo, M. D.

ANDRÉ BUSSON: *Serial Radiographies of the Biliary Ducts Technique*. Arch. Mal. App. Digest. 40, 11, 1170-78. Nov. 1951.

Technique. After a 48 hour fat free diet, the patient is given a double dose of "phenidol." Fourteen hours later, a first radiography is taken in the standing position. Then a second one in dorsal decubitus position. A third one is taken in procubitus with a slight left anterior oblique inclination, so as to clear the gallbladder from the spine and to increase the visibility of the biliary ducts. The distance between the plate and the X-ray tube is one meter. The patient is kept in this position and 150 c.c. of ice cold normal physiological saline is given per os. Five minutes later, he

is given the "Boyden meal" made up of two egg yolks (in some cases fresh cream is added, but without any better results). Then radiographies are taken at intervals of 5-10-15 and 30 and 120 minutes. The patient is removed from the X-ray table after the fourth film. His exact position is then noted in view of his last film (120 minutes). The rapid evacuation of the "Boyden meal" from the stomach is obtained in the following manner: (1) By the procubitus position. It is clear radiologically that the usual dorsal decubitus position hinders to a considerable extent the evacuation of the stomach by holding back the stomach to the left of the spine. (2) By the effect of ice cold normal physiological saline (given before the "Boyden meal") which causes gastric contractions and induces duodenal peristalsis. These duodenal movements stimulate bile excretion. Our serial timing of films was chosen for the following reasons: Five minutes after ingestion of the Boyden meal a normal gall-bladder becomes tense in 90% of cases and in 15% of cases, we have a definite evacuation with a clear picture of the biliary ducts. The first X-ray film allows us to judge the normal onset of evacuation and indicates that the "cholecystokinin" reacts after the usual delays. The second and third films clearly show emptying of the gallbladder and the third one shows that the gallbladder has reached 50% of its initial volume. These last two X-ray films are usually the clearest of the series. After the fourth film i.e. after 30 minutes, usually 85% of the gall bladder volume has been evacuated. In normal cases the emptying of the gallbladder is almost complete by this time. The last film (120 minutes) can be either identical with the fourth one or may be noticeably different—sometimes the picture is smaller with complete disappearance of the opaque matter. In the majority of cases the gallbladder is larger, following a period of rest, due to the dilution of the "phenidol" left over after 30 minutes by the new incoming bile or from a mixture of the new bile and "phenidol."

The first film (5 minutes) indicates whether the gallbladder stimulus is acting normally. The second, third and fourth films (10"-15"-30") will show normal gallbladder evacuation and enable its contractibility and kinesis to be judged. The fifth film (120") gives the picture of a gallbladder at rest and emphasizes the value of its tonicity after evacuation. We can therefore differentiate between kinesis and gallbladder tonicity. Also, by our technique, it is between the first and the fourth picture that the biliary tract is visible; the cystic duct seen in 75% of cases and the common duct in 65% of cases. Systematized serial radiographies must be made if all the information pertaining to the function of the gallbladder and the biliary ducts is to be obtained from cholecystography.

This opinion has been definitely confirmed by Geraldo Siffert who himself uses this method combined with volumetric measures of the gallbladder. It is to be regretted that his important works have not been sufficiently followed in France. For a number of years Boyden in America has been convinced of the utility of multiplying the films in series. Our technique differs from those used by the previously mentioned authors. Geraldo Siffert takes his X-ray films in the procubitus position at 15-60 and 120 minute intervals. We have pointed out the advantage of 5 and 10 minute films with our method of accelerated evacuation and that the

30 minute film can easily replace the 60 minute film—thereby shortening the period of examination on the X-ray table and in the X-ray room. Boyden, on the other hand, takes films every second minute for 60 minutes. He indubitably obtains superior results but this greater number of films seems to us excessive for a first examination.

Our technique is for use as a daily standard technique of gallbladder examination. It consists of eight films, 3 before the "meal," then 5 at the indicated time intervals. This method immobilizes the X-ray room for a relatively short time. It is clear that our technique does not sum up all of gallbladder radiology. If an anomaly is discovered, then Boyden's method will be used together with a series of films to complete the investigation. Because of these techniques, plus the timed duodenal tube as carried out by Varela Fuente and Varela Lopez, we are convinced that we are in a better position to explore the biliary tract and to distinguish with greater facility the difference between an organic lesion and functional disorders. It will also provide more precise information for medical or surgical treatment and our patients will come with a greater sense of security to the operating table, where Caroli's radiomanometry is essential before the actual surgical operation. Following the same radiological procedure, we have examined some of our patients at monthly intervals and have found that the radiological morphology remains the same exactly. In like manner, Gerald Siffert, using his own method, has examined some normal patients twice a year and has obtained the same constant radiological results. *Summary of the article: "Radiographies en série systématisées des voies biliaires" André Bussan—Arch. Mal. App. Digestif T40 N°11—November 1951, p. 1170-1178.*

Guy Albot, M. D.

CATTAN, R., CARASSO, R., FRUMUSSAN, P., HOPPELER, H., PARIENTE P., AND ZERAH, CH.: *Multiple localisations of lymphosarcomatosis (Kundrat's disease) in the digestive tract.* Arch. des Mal. App. Dig. No. 12. 1951, p. 1289.

In this well-illustrated article, the authors describe almost identical observations carried out with three patients suffering from Kundrat's disease. In all three cases, the apparent onset was by way of the pharynx and the ganglions of the neck. A biopsy revealed on each occasion that it was a question of lymphocysto-lymphoblastoma.

In the first case, the radiological examinations of the stomach showed extremely curious images of hypertrophic gastritis which diminished, without disappearing entirely, under the effect of radiotherapy. On rectal examination, a localization in the ano-rectal region, which is clinically silent, was discovered. The autopsy later revealed that the gastric sub-mucosae was infiltrated throughout by the malignant process, whilst the mucous membrane was, in places the seat of a malpighian metaplasia. Furthermore, the spleen and kidneys were the seat of multiple metastases.

In the case of the second patient, after a spectacular improvement of the condition of the pharynx due to radiotherapy, gastric pains and a palpable tumor of the umbilical region appeared. Radiographies showed a magnificent tumoral image of the second portion of the duodenum. There again radiotherapy proved effective.

Later some slight symptoms drew attention to the ano-rectal region. Rectal examination and rectoscopy revealed a relatively soft granulating mass a few centimeters away from the anus. Radiotherapy by way of the sacral tract caused the rapid disappearance of the tumor which left no trace at the autopsy. Death occurred due to hemorrhage following incision of a superficial abscess.

With the third patient, the localization in the stomach after a complete abatement of the pharyngeal symptoms resembled an ordinary cancer of the lesser curvature. There again radiotherapy was momentarily amazingly effective. Furthermore, thirteen centimeters away from the anus, there was a rectal localization which was responsible for disorders which had for a long time been wrongly attributed to chronic amebiasis.

The authors insist on the frequency of multiple metastases of the digestive tract and notably on the necessity of a systematic proctological examination in the case of Kundrat's disease.

Guy Albot, M. D.

LEVIN, E. J. AND FELSON, B.: *Asymptomatic gastric mucosal prolapse.* Radiology, 57, 4, Oct. 1951, 514-520.

Upper gastro-intestinal roentgen studies were performed in 100 patients who had no gastro-intestinal symptoms. Prolapse of the gastric mucosa into the duodenum was encountered in 18 cases. The prolapse was slight in 10, moderate in 5, and marked in 3. No significant increase in frequency of prolapsed mucosa was encountered in any particular systemic disease. Because of the high incidence of this finding in patients without symptoms, it is concluded that the clinical significance of gastric prolapse has been over-emphasized and that it is seldom the cause of symptoms. (The following radiographic criteria for the diagnosis were used—(1) concavity of the base of the duodenal bulb, (2) mucosal folds passing from the stomach into the bulb, (3) inconstant deformity of the base of the bulb caused by the varying degree of the prolapse).

WILSON, E.: *Local methods of treatment of carcinoma of the rectum.* Am. J. Proctology, 2, 3, Sept. 1951, 121-127.

Local excision and suture or diathermy should be employed if localized and low-grade malignant changes have occurred in a pedunculated tumor which was previously benign, provided it is easily accessible from the anus and shows no evidence of extra-rectal spread. Rectosigmoidectomy is indicated if the tumor is too large for local excision. Sometimes local excision or rectosigmoidectomy is indicated in sessile tumors even though highly malignant, if there is additional disease, metastases or short life expectancy, especially where a radical operation would be too difficult, where colostomy is refused or where the patient, because of feeble mentality, would be incapable of managing a colostomy.

HETZEL, P. S.: *Idiopathic hyperlipemia, with a report of two cases occurring in one family, and a review of the literature.* Med. J. Australia, Sept. 15, 1951, 396-399.

This rare disease, of which only 20 cases have been reported, consists in the presence of a very high neutral blood fat, without corresponding increase in

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cholesterol, lecithin, sphingomyelin or cephalin. In the case reported there were no symptoms of any kind. The total serum lipid content was 4540 mg. percent, (normal 450 to 1260). The disease was discovered when the patient offered himself as a blood donor, the serum having a milky appearance. In some cases, the retinal vessels may appear milky (lipemia retinalis). Liver and spleen may be enlarged. Eruptive xanthomata may occur. Glycosuria may be found in some cases. In the present case no special diet was ordered, as the patient seemed quite well. In some cases severe abdominal crises may occur. In these idiopathic cases the accumulation of fat in the blood seems to be due to defective removal of fat from the blood and sluggish deposition in fat depots (retention hyperlipemia).

PARKER, H. W.: *Pilonidal disease—its evaluation and treatment*. Am. J. Proctology, 2, 3, Sept. 1951, 111-120.

Parker recognizes the fact that surgery for pilonidal cyst has been notoriously unsuccessful partly because the cyst is not always entirely removed. Parker has operated on 500 cases using the one technic and his patients have been healed up in from 3 to 5 weeks. The essential point in his technic is the division of the cyst down through the middle followed by complete extirpation of both halves. He dwells on the importance of *micro-aerophilic* hemolytic streptococci in wound infections and sinus infection and also on the efficacy of 2.5 percent tyrothricin as a wet dressing. Sometimes drying fungicidal powders are valuable, or else Desenex. His results are so good that his technic ought to be copied.

FUENTES, B. V., AND LOPEZ, J. V.: *The duodenal drainage in the hepato-cellular jaundice, "hepatocytic jaundice."* Arch. Mal. App. Dig. T. 40. 209-10. 1951. p. 979.

The duodenal drainage is most useful in the *hepatocytic jaundice*.

1)—It allows to measure with precision *how much bile still gets into the duodenum*.

During the period of intense jaundice, the faeces generally are discoloured, putty-coloured, for many days, just as they are observed in the *jaundice from neoplastic obstruction of the common duct*. If the hepatocytic jaundice has begun without either fever or pains, in patients over 50 years of age, it is to be doubted whether a neoplastic obstruction is in existence. The duodenal drainage often permits to solve this doubt. In the neoplastic obstruction, when the jaundice is intense, the *yellow duodenal liquid generally is not obtained*, whereas it is obtained in the hepatocytic jaundice in spite of the faeces being acholic. If the duodenal liquid does not appear yellow spontaneously, we instill through the tube 20 c.c. of a 1% solution of procaine, which permits the getting of the biliary liquid in many cases that originally didn't give it. In the hepatocytic jaundice, it is exceptional to get *colourless* duodenal liquid during the first intubation if the instillation of procaine is made (13% of our cases). But, in a second or third intubation, performed within the space of a week, the *yellow* liquid always appeared in the end, which permitted to discard with certainty the neoplastic origin of the biliary obstruction.

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2)—The duodenal intubation allows us to investigate which is the *functional state of the biliary tree* in the hepatocytic jaundice.

Realized through the new technique indicated by us (Arch. Mal. Appar. Dig. & Nutr. 1950, 39, 797) we have found in 74% of our cases, the signs we have described as typical of the *hypertonic sphincter of Oddi**, which we relate with the duodenitis, so frequent in this affection. The great hypertony of the Oddi often coexists with a severe insufficiency of the hepatic parenchyma. Moreover, it may be accompanied by the symptoms peculiar to the jaundice caused by biliary mechanical obstruction (itching, hepatic colics), and by biochemical blood changes, customary in such jaundice (moderate increase of the *free cholesterol* and of the *alkaline phosphatase of the serum*).

Test of the emptying of the gall-bladder.

It is admitted that, in the hepatocytic jaundice, it is *not possible* to obtain gall-bladder "B" bile after the instillation into the duodenum of the olive oil or the magnesium sulfate. But, with the instillation of procaine, we have obtained a *positive gall-bladder emptying in half of our 30 cases* in full jaundice (weak answer in 5 cases, *clear* in 6; and with *black bile* in 4 cases).

3) The duodenal drainage is very useful as a *therapeutical measure* in the severe hepatocytic jaundice. But it has proved still more efficacious to us since we have instilled, during the intubation, procaine at 1% (20 c.c. every time) when there is an hypertonic Oddi. We complete this treatment by giving, by the mouth, 0.2 gms. of procaine (as a solution or in soluble tablets) 20 minutes before meals, two to four times daily. The procaine is well tolerated by these patients, even in cases of severe hepatocytic insufficiency.

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*a) a total absence, or the obtaining of a very small quantity of duodenal liquid during the common duct time, that is after the tube has been introduced in D 2; b) after instilling oil or magnesium sulfate into the duodenum, the time of the closed Oddi, that is, the time before the bile runs again out of the tube, which normally lasts 3 to 6 minutes, extends notably. When more than 20 minutes elapse, we proceed to the instillation through the tube of 20 c.c. of procaine at 1%, which usually provokes, in the course of 1 to 2 minutes, the reopening of the Oddi, with the renewing of the bile flowing.

DAVIS, M. C.: *The role of dental sepsis in systemic disease*. Med. J. Australia, Sept. 15, 1951, 349-353.

One cannot study this article by Davis without being confirmed in his convictions that dental infection may, and does, play a major role in systemic disease. Davis emphasizes that in all cases of illness, the "soil" is of importance because different persons react differently to infection. He cites rheumatic fever as a special type of reaction of the strept. hemolyticus, of which not everyone is capable. Incidentally this destroys the universality of Koch's postulates because we cannot reproduce rheumatic fever by injecting the S. hemolyticus into animals. All collagen diseases fall into a similar category. Every case of systemic disease should be examined for dental infection because, as Davis shows by several representative case reports, the removal of diseased teeth frequently cures the systemic disease, of whatever variety it may seem to be. Fevers of obscure origin,

many respiratory syndromes, some cases of chest pain, myositis and fibrositis (simulating angina) frequently recover after the removal of dental infection. Bacterial endocarditis is very clearly related today to dental infection. In cases of systemic disease which represent general reaction of a dental infective focus, no cure is possible until the focus is removed. As Davis states, there is need for a closer cooperation between doctors and dentists and for a better understanding of both professions of the potential seriousness of dental infection.

AMIES, A. B. P.: "Out of focus"—medicine or dentistry? *Med. J. Australia*, Sept. 15, 1951, 353-355.

Amies, professor of Dental Science at the University of Melbourne, says that in Australia Dentists are taught much more about general health than physicians are taught about teeth. He believes that dental focal infection is a genuine source of general disease, and believes the dentist and not the physician should be the final arbiter in assessing oral foci of infection. He talks at some length about caries, pulp infection, granulomata, cysts and chronic abscesses as well as gingivitis, pyorrhea and Vincent's infection. He thinks that, where possible, every patient before taking a general inhalation anesthetic should have a careful dental prophylaxis because of the risk of micro-organisms gaining access to the bronchi and lungs.

POPONA, A. M. AND STONE, A. M.: *Hiatus hernia and gastrointestinal diverticulosis*. *Northwest Med.*, 50, 10, October, 1951, 773-4.

Out of 3,000 gastrointestinal x-ray examinations made in the past 2 years at St. Luke's Hospital, Boise, Idaho, 60 patients were found to have hiatus hernia, and of these 60 patients, no fewer than 28 were found also to have diverticula of the duodenum, jejunum or colon. By far the great majority presenting both lesions were in their sixth, seventh and eighth decades of life. The authors offer the hypothesis that these conditions occur as a result of aging and general deterioration and weakening of body tissues, particularly the muscle fibers of the diaphragm and the intestinal walls. They do not touch the matter of treatment as this is for joint consideration by the physician and the surgeon.

WELBOURN, R. B., BUTLER, T. J., CAPPER, W. M.: *Discussion on post-gastrectomy syndromes*. *Proc. Roy. Soc. Med.*, 44, 9, Sept. 1951, 773-778.

Only 5 percent of patients, following subtotal gastrectomy for ulcer, have really severe symptoms, although many others present the syndromes in a mild degree, dumping, anemia, vitamin-B deficiency and loss of weight. The operation in which $\frac{3}{4}$ of the stomach is removed results in rapid gastric emptying, reflux of duodenal material, frequent achlorhydria and the removal of the intrinsic factor. Especially after a Polyn subtotal gastrectomy we are likely to get the "dumping syndrome (post-prandial fullness, sleepiness, nausea, sweating, and palpitation)". This syndrome has nothing to do with the blood sugar curve, although there is a hypoglycemic syndrome too, which, if it occurs, does so 3 hours after eating. The dumping

syndrome is probably due merely to increased tension and motor activity in the bowel and not to distension. Undiluted chyme may, by its hypertonic nature, cause diarrhea or steatorrhea. These patients should be fed fat more slowly, and emulsifying agents such as "Tween 80" are of value. The main problem in gastric surgery today is to find a method of controlling peptic ulceration without interfering with the reservoir function and normal emptying mechanism of the stomach.

The post-gastrectomy syndrome does not follow the Billroth I operation and is rare following gastroenterostomy or total gastrectomy,—a surprising observation if one follows the popular views today (Butler). The feeling of fullness is due to jejunal filling and is unaffected by posture. The vasomotor symptoms are due to gravity and are relieved by lying down.

The stretching of the unsupported gastric remnant by the food load is a very important factor in producing the early syndrome (Capper). By putting a strong silk ligature around the mass of tissue surrounding the left gastric artery and leaving the end long, so that at the end of the operation the lesser curve at the angle of the anastomosis can be drawn up to this point, one is able largely to prevent the syndrome.

RITVO, M., COTTER, T. P. AND ZAMCHECK, N.: *Early roentgen diagnosis in acute bleeding from the upper gastrointestinal tract. II. Roentgen aspects*. *Am. J. Roentgen. & Rad. Therapy*, 66, 5, Nov. 1951, 728-742.

The general import of this article is to the effect that barium meal studies do not need to be postponed, and indeed ought not to be postponed because of active hemorrhage in the upper gastrointestinal tract. In 52 bleeding patients, emergency x-ray examination of the esophagus, stomach and duodenum was done as soon as possible. In 42 percent the examination was done within 24 hours; in 63.5 percent within 48 hours and in about 83 percent in less than 72 hours after admission to hospital. Three patients were too ill to stand; 44 could stand but mechanical pressure could not be used; 5 underwent complete x-ray study including palpation and mechanical pressure. Small amounts of the opaque meal proved more satisfactory for the demonstration of most lesions. There were no serious complications attributable to the roentgen studies. Early x-ray examination may prevent unnecessary laparotomy, reduce time-consuming exploratory procedures and facilitate surgical treatment. Sometimes the early determination of the cause and site of the bleeding may prove to be life-saving.

CHAUDHURI, S.: *Vitamin B₁₂ in megaloblastic anemia of pregnancy and tropical nutritional macrocytic anemia*. *Brit. Med. J.*, Oct. 6, 1951, 825-828.

There has been considerable debate about the value of vitamin B₁₂ in the megaloblastic anemia of pregnancy but the author successfully treated 16 cases of the disease in India with this vitamin. Out of 5 cases of tropical megaloblastic anemia, four responded to vitamin B₁₂ and one showed better response to subsequent folic acid treatment. (In America, folic acid seems more satisfactory in treating the megaloblastic anemias of pregnancy—Reviewer).

TORGENSEN, J.: *Suprahepatic interposition of the colon and volvulus of the cecum*. Am. J. Roentgen. and Rad. Therapy, 66, 5, Nov. 1951, 747-751.

Interposition of the colon above the liver was noted in 0.25 percent of films in mass x-ray examinations of the chest. Perhaps in slightly more than half the cases the condition is permanent. The condition is more frequent in males, especially as they grow old. In men the colon is displaced to the right and above the liver while in women it is in front of the liver in not a few cases. The condition is especially frequent among psychotics and mental defectives and among these patients, ileus and volvulus are relatively frequent. Two cases are recorded suggesting a genetic relation between interposition, volvulus of the cecum and visceral asymmetry.

LEWIS, H. P.: *Pain in acute and chronic diseases of the liver*. Ann. Int. Med., 35, 4, October 1951, 878-888.

This is a valuable article because it emphasizes something of which clinicians are not too well aware, viz., that liver disease can and usually does produce pain without requiring complications. The author describes the liver pain in hepatitis, in cirrhosis, primary liver cancer and hepatic abscess. The pain patterns in these diseases are often clear enough to be of diagnostic help. Distention of the capsule, the usually accepted cause of liver pain, cannot explain all cases and it is likely that pain is often due to inflammation of the hepatic parenchyma. Right supraclavicular and shoulder pain occurs in some cases of gall bladder and parenchymatous liver disease. Sharp fist percussion over the liver may sometimes produce a deep-seated, aching pain that persists for a short time. This is of diagnostic value in hepatitis and pyogenic abscess.

SINCLAIR, W. J.: *Pleomorphic adenoma and adenocarcinoma of the parotid gland*. Northwest Med., 50, 11, 825-4.

Mixture of epithelial and mesenchymal elements in tumors of the parotid has caused confusion. Non-epithelial material is inert, not capable of reproduction, and is not present in metastases. The term *mixed tumor* should be replaced by *pleomorphic adenoma* and *adenocarcinoma*. Enucleation is inadequate. Such tumors should always be treated by total extirpation of the parotid or by lobectomy.

WINHAM, A. J. AND PECHSTEIN, G. R.: *Clinical and roentgen observations of a newly perforated peptic ulcer*. Radiology, 57, 4, Oct. 1951, 551-553.

The authors had the possibly unique experience of having a duodenal ulcer perforate during fluoroscopic examination. Barium lying outside the G. I. tract was noted at once. Within 3 hours free air was demonstrated in the peritoneal cavity. Operation proved the diagnosis. Two weeks after the operation some streaks of barium were plainly visible in the peritoneal cavity.

GOULSTON, S. AND SMITH, M.: *Intrahepatic biliary tract obstruction of unknown origin: the so-called cholangiolitic hepatitis*. Med. J. Australia, Sept. 8, 1951, 313-317.

Two cases are described of a type of intrahepatic obstructive

jaundice of unknown causation which seemed to correspond to the so-called cholangiolitic hepatitis of Watson and Hoffbauer (Ann. Int. Med., XXV, 1951). After two years' observation, Case I would still appear to fit this diagnosis, but Case II has revealed itself as carcinoma, the site and origin of which still is obscure. The diagnosis of cholangiolitic hepatitis should not be readily accepted in relation to a patient over 40 years of age. The patients concerned were operated on, and it is suggested that surgery might be considered in cases of chronic hepatitis in which obstructive features are present.

NORCROSS, J. W., FELDMAN, J. D., BRADLEY, R. F. AND WHITE, R. M.: *Liver function: an attempt to correlate structural change with functional abnormality*. Ann. Int. Med., 35, 5, Nov. 1951, 1110-1116.

A series of 82 liver biopsies, surgically removed, was studied to correlate function and structure. A battery of liver function tests was done on each and the results compared with the microscopic findings of the liver biopsy. An elevated serum bilirubin or an elevated alkaline phosphatase level was associated with periportal inflammation and periportal fibrosis. An elevated serum bilirubin was also associated with a bile duct increase and the presence of bile thrombi. Similarly, elevated urinary bilirubin indicated the presence of bile thrombi, periportal fibrosis and bile duct increase. Using routine histological methods, morphological changes in the hepatic cells were slight and could not be correlated with abnormal function tests.

SUGAI, T. AND TSUBOI, A.: *Some observations in a patient with external pancreatic fistula*. Yokohama Med. Bull., 1, 2, Dec. 1950, 77-82.

Using a patient with an external pancreatic fistula, it was found that there was no fundamental difference in the secretions in response to carbohydrate or protein. The quantity of secretion was parallel to the time of secretion, the curve being parabolic. Pancreatic secretion was found to be due to absorption of glucose, certain amino acids and lipoids, while fats and their derivatives had no influence. The food must proceed as far as the duodenum to stimulate secretion. The gastric acidity had no influence other than free HCl which the authors believe to be an entirely different mechanism from that due to food. Regardless of the volume of secretion, the amount of enzymes and inorganic material is constant. Vagus stimulation increased secretion, while sympathetic stimulation decreased it. They found it possible to extract strong preparations of amylase and trypsin with relative ease.

WHITE, R. J.: *Congenital lesions of the alimentary tract in infants and children*. Texas State J. Med., 47, 11, Nov. 1951, 740-744.

This paper is a discussion of pyloric stenosis, intestinal atresias, malrotation of the intestine, abdominal wall defects, intussusception, atresia of the anus, sacral teratomas, cystic lymphangioma of the mesocolon, congenital atresia of the esophagus, diaphragmatic hernia, congenital cystic dilatation of the common bile duct, atresia of the bile ducts, omphaloceles and an unusual anomaly of the umbilicus.

NATIONAL GASTROENTEROLOGICAL ASSOCIATION 1952 AWARD CONTEST

The National Gastroenterological Association again takes pleasure in announcing its Annual Cash Prize Award Contest for 1952. One hundred dollars and a Certificate of Merit will be given for the best unpublished contribution on Gastroenterology or allied subjects. Certificates will also be awarded those physicians whose contributions are deemed worthy.

Contestants residing in the United States must be members of the American Medical Association. Those residing in foreign countries must be members of a similar organization in their own country. The winning contribution will be selected by a board of impartial judges and the award is to be made at the Annual convention Banquet of the National Gastroenterological Association in October of 1952.

Certificates awarded to other physicians will be mailed to them. The decision of the judges will be final. The Association reserves the exclusive right of publishing the winning contribution, and those receiving Certificates of Merit, in its Official Publication, The Review of Gastroenterology.

All entries of the 1952 prize should be limited to 5,000 words, be typewritten in English, prepared in manuscript form, submitted in five copies accompanied by an entry letter, and must be received not later than 1 September 1952. Entries should be addressed to the National Gastroenterological Association, 1819 Broadway, New York 23, N. Y.

PARKE, DAVIS & COMPANY PROMOTES WALTER A. HOWELL, 39, TO SUPERINTENDENT OF PLANNING AND DISTRIBUTION

Promotion of Walter A. Howell, 39, to superintendent of the planning and distribution division at Parke, Davis & Company was announced recently by Dr. Harvey M. Merker, director of inventory control and chemical and pharmaceutical consultant.

Howell started as a bottle washer in the ampoule department in 1934. Working at Parke-Davis days, he took night courses at Wayne University, graduating in 1938 with a

bachelor of science degree. In 1939 and 1940, he took post-graduate courses there at night.

Meanwhile, at Parke-Davis, he advanced to section head in the drug and chemical department in 1936, and to section head in the biological division in 1938. From 1942 to 1945, he was a special production engineer for that division. He was transferred in 1945 to the general superintendent's office and became assistant to the superintendent of production in 1947, holding that post until his latest promotion.

Dr. Merker explained that Howell would be responsible for the planning functions in the Detroit and Holland (Mich.) plants and for the distribution of more than 1,000 Parke-Davis products to the 30 branches in the United States, and to Canada and Panama.

Howell is married; has two sons; and lives at 14243 Cherrylawn, Detroit.

BENZIDINE

A specially purified grade of benzidine for use in determining the presence of blood, and also for the micro-determination of hemoglobin in blood samples, is among a group of ten compounds which have just been added to the list of more than 3500 Eastman Organic Chemicals now available.

The special benzidine is designed as Eastman Organic Chemical X33. It will be sold for \$5.50 per 100 grams. Abstracts describing the use of this product are available on request to Distillation Products Industries Eastman Organic Chemicals Department, Rochester 3, New York.

PROCESSED FILMS TO BE RETURNED BY FIRST-CLASS MAIL BY KODAK

Starting July 7 and until further notice, the Eastman Kodak Company will return all processed Cine-Kodak Films and Kodachrome Films 135, 335, and 828, to its customers by *first-class mail*, the company has announced.

Previously, such processed films have been returned by third-class mail unless the owner had requested and paid for better mail service.

No additional charge will be made for the new service. However, if the customer wishes to have his films returned by air mail or special

delivery rather than by straight first-class mail, such special mail service charges must be prepaid when the film is sent in for processing.

The change from third-class to first-class service is being undertaken, the company stated, to assure customers of the best possible service during the summer and fall when record receipts of film for processing are expected at Kodak laboratories.

Since the change will be effected before the information about mail service packed with Kodak Films can be changed, the company is asking its dealers to tell their customers that it is no longer necessary to enclose additional postage to secure the return of films by first-class mail.

The company is also recommending to all picture-takers that they use first-class or better mail service in sending their films to Kodak Processing Laboratories. This will insure them a quicker round trip and will enable them to see their pictures sooner.

The new service will be provided from all Kodak Processing Laboratories in the United States and Hawaii.

A. H. ROBINS CO., INC.

Further investigation of the synergistic action of para-aminobenzoic acid and cortisone in the treatment of rheumatoid arthritis has been made possible through a grant of \$5,500 by the A. H. Robins Co., Inc., of Richmond, Va., to Dr. Leon L. Wiesel of the Brooklyn Hospital, Brooklyn, New York.

Seeking a non-toxic agent which acts synergistically with a low dosage of cortisone to produce and maintain remission without side reactions, Dr. Wiesel and two colleagues reported in the American Journal of the Medical Sciences 222:243, 1951) that para-aminobenzoic acid appears to be such an agent.

In the current study, according to Dr. William R. Bond, director of clinical research for the Robins Company, Dr. Wiesel is undertaking first to establish by animal experimentation the relationship between para-aminobenzoic acid and glutathione, a tissue enzyme or catalyst which apparently is necessary for tissue respiration. Gluta-

thione is stored, along with ascorbic acid, in the adrenal cortex, and like ascorbic acid may be a measure of adreno-cortical activity.

Following this preliminary work, Dr. Wiesel will conduct various clinical investigations, using para-aminobenzoic acid in the form of Pabalate (Robins).

PYRICIDIN—NEW ANTI-TB DRUG

The important new anti-tuberculosis drug, isonicotinic acid hydrazide, has been announced by Nepera Chemical Co., Inc., as now available for prescription use—as Pyridin. Complete information on its laboratory and clinical background has been supplied to all physicians and retail pharmacists.

The Nepera firm's interest in the chemotherapy of tuberculosis goes back over a decade, when they instituted a pioneering research program encompassing the synthesis and evaluation of hundreds of potential anti-TB agents. In this program, their twenty-five years of specialization in the field of pyridine compounds, and their position as one of the largest manufacturers of isonicotinic acid derivatives has stood them in particularly good stead.

CHARLES E. MORTON

Appointment of Charles E. Morton as Kansas City division manager has been announced by E. F. Heffner, Jr., vice president and sales manager of the A. H. Robins Co., Inc., of Richmond, Va. Mr. Morton, formerly of Oklahoma City, took up his duties at Kansas City on July 1.

The new Robins division manager was born in Perryville, Mo., the son of a pharmacist. He was graduated from the Kansas City College of Pharmacy and was pharmacist and store manager for the Crown Drug Co. in that city for several years. In wartime service with the Field Artillery and Air Corps, he rose to the rank of captain. He is married and has three children.

Mr. Morton has been a medical service representative for the Robins Company since 1946 and became a supervisor in the Kansas City Division last October.

"CITRUS FRUIT AND DENTAL HEALTH" REPORTS ON RECENT STUDIES

Thirty-seven references to scientific papers published within the past five years on the relation of vitamin C and citrus fruits to dental health, along with many classical references, are included in a brochure which the Florida Citrus Commission, Lakeland, Fla., has sent to the nation's 80,000 practicing dentists.

Entitled "Citrus Fruit and Dental Health," the booklet summarizes recent investigations in sections on diet and tooth development, the role of citrus in caries control, vitamin C deficiency and periodontal disease, and the use of citrus fruits in oral infections and following extractions.

Included are reports of controlled studies of gum lesions in subjects receiving varying amounts of ascorbic acid. Various authorities suggest a wider prevalence of vitamin C deficiency among various groups than has commonly been suspected. For instance, a study of meals served in a group of college dining halls indicated that the food as served included adequate vitamin C in 48 out of 125 days and that on only two days was an adequate level reached without the use of citrus fruits.

Also contained in the booklet are references to recent reports showing a high retention of vitamin C in canned citrus juices and frozen concentrate. Charts and tables depict the recommended daily allowances of the National Research Council for specific nutrients, list the nutritional contents of citrus fruits and illustrate the physiologic function of vitamin C and the chronology of tooth development.

An introductory statement, after citing the importance of vitamin C in the pre-eruptive development of the teeth, goes on to say that diet also appears to affect the fully formed tooth in two ways.

"First," it is stated, "the health of the saliva, which may act as a protective mechanism against caries, depends to a large extent on a well-balanced diet, including vitamin C. Second, the oral tissues and bones which—by adequate or inadequate support of the teeth, by good or faulty occlusion, by resistance or non-resistance to infection

—also influence the teeth for better or worse, are dependent on bodily nutrition. There is also general agreement that periodontal disease develops into much more severe conditions in the presence of C-avitaminosis."

The Journal of the Florida State Dental Society (23:2:15, April 1952) states: "The booklet is tastefully and effectively designed and contains resumes of the experimental work done on dental disease in relation to vitamin C and citrus fruit. Numerous charts and diagrams make the presentations quite effective and the bibliography is valuable for the research man. The book is written so that an intelligent patient could understand it and it should be invaluable for patient education."

COMMENTS FROM DENTISTS ON "CITRUS FRUIT AND DENTAL HEALTH"

Mankato, Minnesota: "Your brochure, 'Citrus Fruit and Dental Health,' is a most valuable addition to the library of every practicing dentist. In giving out the contained information you are doing a distinct service to the dental profession as well as to the general public. I have maintained for many years that Vitamin C in the citrus fruits was the best source for both old and young patients. It not only prevents decay of teeth in young patients but prevents pyorrhea and other gum troubles in middle-aged and older people. In my family we get oranges by the crate or bushel."

Cut Off, Louisiana: "I sincerely feel that your brochure is outstanding. Congratulations to the Florida Citrus Commission upon the publication of this gem on dental health."

Worcester, Massachusetts: "Congratulations on your excellent presentation of the inestimable importance of nutrition to dental health as defined in the brochure, 'Citrus Fruit and Dental Health.' Its educational material is of such a helping nature that I would like an additional copy for my personal files. The original booklet is displayed in my reception room for patient perusal and education."

Los Angeles, California: "Your brochure on 'Citrus Fruit and Dental Health' is exceptionally attractive and the contents are very educational. It will be placed on a read-

ing table in my reception room. I am very fond of Florida oranges and grapefruit. Just because I live in California I want to be broad-minded about your citrus fruits in Florida. As far as I am concerned, there is no competition, and quite a few of us are willing to give you thousands of inhabitants from our growing population."

**RALPH G. SICKELS OF
PARKE, DAVIS & COMPANY
SELECTED NATIONAL DI-
RECTOR OF MEDICAL EX-
HIBITORS' ASSOCIATION**

Chicago—Ralph G. Sickels, director of advertising and public relations for Parke, Davis & Company, has been elected to a two-year term as a national director of the Medical Exhibitors' Association, Inc.

The organization met here during the 101st annual meeting of the American Medical Association.

A native of Indianapolis, Sickels attended public schools there, and he was graduated from Wesleyan University, Middletown, Conn., in 1914. After two years in the Army, he spent about a year with a small Boston advertising agency. He joined Parke-Davis in 1920 and became advertising manager nine years later. He has been director of advertising and public relations since Jan. 1, 1952. Among his present responsibilities is the chairmanship of the Parke-Davis exhibit committee.

The Medical Exhibitors' Association includes any ethical manufacturer or distributor of products or services used or prescribed by the medical, hospital, dental and allied professions, and who exhibit at conventions in these fields.

**RUBBER IN THE MEDICAL
FIELD**

Ever since the discovery of vulcanization in the early 19th century, rubber has played a basic role in the advancement of surgery and medicine.

It has been particularly effective as an aid in training. With the intensive educational work in medical training now being carried out by such bodies as UNESCO, the application of rubber in this area becomes more important.

In a thorough-going and illustrat-

ed review of rubber's place in the medical field, the current issue of *Rubber Developments* discusses some of rubber's latest training applications. The article also discusses current use of rubber in bandages, chiropody, catheters and surgical tubing, surgical gloves and other medical applications.

The issue of *Rubber Developments* in which this material appears is available without charge from the Natural Rubber Bureau, 1631 K Street, N. W., Washington 6, D. C.

CIRRHOSIS OF LIVER

Chicago, Ill.,—"Decisive evidence, indicating that a large proportion of cases of cirrhosis of the liver may be alcohol-induced is revealed in a resumé of recent findings of distinguished European scientists," declares a review of this testimony just released by the American Business Men's Research Foundation.

"In contrast to propaganda of moderationists, the conclusion of these European scientists assembled by Ernest Gordon is that from 50 to 100% of deaths from cirrhosis of the liver, over various recent periods, have been found to have been induced by consumption of alcoholic beverages.

"Summed up in an important French volume *L'Alcoolisme*, Prof. Dr. Paul Perrin, who published this survey in 1950, quotes from eight French medical authorities who conclude that cirrhosis and stomach ulcers are among the most significant ailments of alcoholics.

"The findings of these French scientists are strongly in agreement with the reports of the Registrar-General of Births, Deaths, and Marriages, in England and Wales. Therein it is stated that among brewers and saloonkeepers, deaths from liver diseases are nearly seven-fold greater than among the people taken as a whole."

**CORTROPHIN 'ORGANON'
PROVIDES A STABLE ACTH
SOLUTION**

Organon Inc., of Orange, N. J., has just announced the availability of Cortrophin, an improved form of its adrenocorticotrophic hormone preparation. Cortrophin—the first ACTH preparation in the world—was first marketed by Organon in 1945.

Cortrophin is supplied in two strengths: 25 U. S. P. unit vials and 40 U. S. P. unit vials. These vials are packaged with a 5-cc vial of a special Cortrophin solvent to enable greater ease in varying the dosage. The reconstituted Cortrophin solution remains stable for at least a month at room temperature.

Adrenocorticotrophic hormone is the body's natural stimulant of the adrenal cortex—the energy mobilizer. Cortrophin is indicated in the treatment of all stressful conditions which respond to ACTH therapy: such conditions, for example, as shock, coma, allergic reactions, collagen diseases, inflammatory skin and eye diseases, ulcerative colitis, and others. The dosage of Cortrophin must be individualized to the needs of the patient.

As with all Organon preparations, Cortrophin is never advertised to the laity. Descriptive literature is available on request.

**MERCUHYDRIN NOW AVAIL-
ABLE IN NEW "COLOR-
BREAK" AMPULS**

Mercurydrin is now available in Kimble Glass Company's new "Color-Break" ampuls according to an announcement by Lakeside Laboratories, Inc., Milwaukee, Wisconsin. These ampuls are easy to manipulate and eliminate the need of a saw. Breaking cleanly and without difficulty at a point in the neck indicated by a color line, the ampuls mean more speed and efficiency to the doctor in handling Mercurydrin.

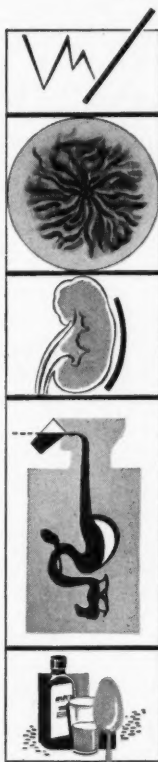
This innovation is in keeping with Lakeside's policy of staying abreast of the latest developments in the pharmaceutical field. Mercurydrin is the first Lakeside product to be converted to "Color-Break" ampuls and will be followed as rapidly as possible by the balance of Lakeside's injectable ethical line.

**PHILIP R. MARSH, 40,
NAMED FIELD MANAGER
FOR PARKE, DAVIS & COM-
PANY AT CINCINNATI**

Detroit—Appointment of Philip R. Marsh as field manager for the Cincinnati branch of Parke, Davis & Company, maker of over 1,000 different pharmaceutical products, was announced recently by Carl Johnson, U. S. sales manager.

Marsh joined the Detroit branch

FOR THE PEPTIC ULCER PATIENT
 "DOUBLE-GEL ACTION" **AMPHOJEL**



relieves pain promptly

promotes rapid healing

no kidney damage

never causes alkalosis

no acid rebound

pleasant to take

stops gastric corrosion

provides a soothing protective coating over the ulcer

imposes no added burden on kidney function

buffers gastric contents moderately; permits normal neutralization of alkaline secretions of upper intestine

even in excessive doses. Does not cause unphysiologic alkalinity and consequent acid secretory response

smooth, creamy, pleasing taste and texture



SUPPLIED: Liquid, bottles of 12 fl. oz. Also available: Tablets of 5 grains and 10 grains

After 15 years of clinical use, still a leading prescription product for peptic ulcer—



AMPHOJEL®

ALUMINUM HYDROXIDE GEL • ALUMINA GEL WYETH

Wyeth Incorporated, Philadelphia 2, Pa.



"I clean the poisons out every day," he says—but he doesn't realize he is whipping a tired, irritated bowel.

Put this character on a treatment of Turicum. Explain to him it is not a one-shot cathartic but a restorative treatment that should be kept up for several days to help the bowel back to normal reflex peristalsis.

TURICUM[®]

lubricoid action without oil

It is pleasant and easy to take.

WHITTIER LABORATORIES

CHICAGO 11, ILLINOIS

A DIVISION OF NUTRITION RESEARCH LABORATORIES, INC.

of Parke-Davis in 1942 in a sales capacity, and he has served with headquarters in Cleveland, Ohio, until his present appointment.

Born in Milwaukee, Wis., in 1912, Marsh was graduated from the University of Pittsburgh College of Pharmacy in 1934. He was employed in drug stores of the Pittsburgh area for several years.

Marsh is married and has two children.

HORACE L. JOHNSON PROMOTED TO FIELD MANAGER FOR PARKE, DAVIS & COMPANY AT BOSTON BRANCH

Detroit—Appointment of Horace L. Johnson as field manager for the Boston branch of Parke, Davis & Company was announced recently by Carl Johnson, U. S. sales manager.

Johnson has been associated with Parke-Davis since 1941, except for four years in which he served as a captain in the U. S. Army. He joined the company as a medical service man in New Hampshire. After World War II, he was assigned to similar work in the Boston area.

A 1939 graduate of the Massachusetts College of Pharmacy, Johnson began his professional career in New Hampshire.

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AMER. JOUR. DIG. DIS.

NEW Pfizer Steraject Syringe

holds 2 cartridge sizes

Steraject*

sterile, single-dose
disposable cartridges

the most
complete line
of single-dose
antibiotic
disposable
cartridges



Steraject Penicillin G
Procaine Crystalline
in Aqueous Suspension
(300,000 units)



Steraject Penicillin G
Procaine Crystalline
in Oil with 2% Aluminum
Monostearate (300,000 units)

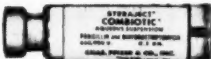


Steraject Penicillin G
Procaine Crystalline
in Aqueous Suspension
(1,000,000 units)

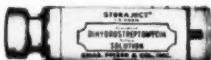


2 cartridge sizes for only 1 syringe!

Steraject Combiotic*
Aqueous Suspension
(400,000 units Penicillin G
Procaine Crystalline,
0.5 Gm. Dihydrostreptomycin)



Steraject Dihydrostreptomycin
Sulfate Solution (1 gram)



Steraject Streptomycin
Sulfate Solution (1 gram)



two cartridge sizes permit full
standard antibiotic dosage
cartridges individually labeled
ready for immediate use
no reconstitution

for full details, ask your Pfizer
Professional Service Representative

Steraject Cartridges:
each one supplied with
sterile needle, foil-wrapped

introduced by **Pfizer** world's largest producer of antibiotics

*TRADEMARK, CHAS. PFIZER & CO., INC.

ANTIBIOTIC DIVISION • CHAS. PFIZER & CO., INC. • BROOKLYN 8, N. Y.

Excessive Perspiration

The hands of a girl of 17 with a history of hyperhidrosis of 9 years' duration. The sweating was a definite social handicap.



The same patient 45 minutes after taking 100 mg. of Banthine. She has been maintained on a schedule of 50 mg. three times daily. Illustrations courtesy of Keith S. Grimson, M.D.



Hyperhidrosis constitutes a serious mental as well as physical handicap. Its treatment is therefore highly important.

The control of this obstinate condition by Banthine is accomplished by the true anticholinergic action of the drug—an action which has made Banthine one of the outstanding drugs of recent years.

BANTHINE[®] BROMIDE

Brand of Methantheline Bromide

ORAL...PARENTERAL



RESEARCH IN THE SERVICE OF MEDICINE **SEARLE**